Inhibition of WEE1 Is Effective in TP53- and RAS-Mutant Metastatic Colorectal Cancer: A Randomized Trial (FOCUS4-C) Comparing Adavosertib (AZD1775) With Active Monitoring

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PURPOSE Outcomes in RAS-mutant metastatic colorectal cancer (mCRC) remain poor and patients have limited therapeutic options. Adavosertib is the first small-molecule inhibitor of WEE1 kinase. We hypothesized that aberrations in DNA replication seen in mCRC with both RAS and TP53 mutations would sensitize tumors to WEE1 inhibition.

METHODS Patients with newly diagnosed mCRC were registered into FOCUS4 and tested for TP53 and RAS mutations. Those with both mutations who were stable or responding after 16 weeks of chemotherapy were randomly assigned 2:1 between adavosertib and active monitoring (AM). Adavosertib (250 mg or 300 mg) was taken orally once on days 1-5 and days 8-12 of a 3-week cycle. The primary outcome was progression-free survival (PFS), with a target hazard ratio (HR) of 0.5 and 80% power with a one-sided 0.025 significance level.

RESULTS FOCUS4-C was conducted between April 2017 and Mar 2020 during which time 718 patients were registered: 247 (34%) were RAS/TP53-mutant. Sixty-nine patients were randomly assigned from 25 UK hospitals (adavosertib = 44; AM = 25). Adavosertib was associated with a PFS improvement over AM (median 14.0 months; HR = 0.35; 95% CI, 0.18 to 0.68; P = .0022). Overall survival (OS) was not improved with adavosertib versus AM (median 14.0 v 12.8 months; HR = 0.92; 95% CI, 0.44 to 1.94; P = .93). In prespecified subgroup analysis, adavosertib activity was greater in left-sided tumors (HR = 0.24; 95% CI, 0.11 to 0.51), versus right-sided (HR = 1.02; 95% CI, 0.41 to 2.56; interaction P = .043). Adavosertib was well-tolerated; grade 3 toxicities were diarrhea (9%), nausea (5%), and neutropenia (7%).

CONCLUSION In this phase II randomized trial, adavosertib improved PFS compared with AM and demonstrates potential as a well-tolerated therapy for RAS/TP53-mutant mCRC. Further testing is required in this sizable population of unmet need.

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INTRODUCTION

Targeting the cellular DNA damage response (DDR) has been an effective therapeutic strategy in several tumor sites, including ovarian and pancreatic cancer.1,2 These agents can be used as monotherapy in cancers with defective DDR, where we might anticipate a synthetic lethality interaction: two pathways together perform an essential function, and the loss of one pathway (eg, because of mutation) is tolerated but the loss of both pathways leads to cell death.3 WEE1 is a nuclear tyrosine kinase that has a central role in cell cycle regulation, including being the key regulator of the G2/M checkpoint through actions on CDK1,4 optimizing DNA-histone stoichiometry before mitotic entry5 and modulation of CDK1/2 during the intra-S phase to block replication initiation.6 Inhibition of WEE1 causes unscheduled entry into mitosis, aberrant firing of replication origins leading to dNTP (Dithiobis [5-nitro-pyridine]) shortage and replication stress,4 and accumulation of DNA damage during S phase, leading to increased reliance on the G1/S checkpoint.4 Adavosertib (AZD1775) is the first small-molecule inhibitor of WEE1 kinase and has been tested in combination with chemotherapy and radiotherapy,4,7 but more recently as monotherapy to generate synthetic lethality in tumors with DDR defects.6 There has been limited investigation into agents targeting the DDR in metastatic colorectal cancer.
CONTEXT

Key Objective
To test if adavosertib, which is a small-molecule inhibitor of the WEE1 kinase, is effective as monotherapy in patients with RAS/TP53-mutant metastatic colorectal cancer (mCRC) as maintenance therapy following induction chemotherapy.

Knowledge Generated
In this phase II randomized trial, adavosertib was well-tolerated and improved progression-free survival in RAS/TP53-mutant mCRC compared with active monitoring. Treatment effect may be affected by primary tumor location and KRAS subtype, with greater benefit seen in left-sided cancers and those with KRAS codon 12/13 mutations. RAS/TP53 subgroup is a distinct moderately poor prognostic population.

Relevance
Adavosertib is a promising therapeutic agent in patients with RAS/P53-mutant mCRC, a poor prognostic population of unmet need, and was well-tolerated. This study demonstrates the potential of targeting the DNA damage response pathway in mCRC, which should be a research priority. Future studies of adavosertib should stratify patient outcomes according to primary tumor location and RAS subtype.

METHODS

Trial Approvals, Patient Eligibility, and Recruitment
The trial and subsequent amendments were approved by the UK National Ethics Committee Oxford—Panel C (reference 13/SC/0111) and by the relevant regulatory body MHRA (CTA No. 20363/0400/001 and EudraCT No. 2012-005111-12).

Patients age more than 18 years with newly diagnosed mCRC were registered into the FOCUS4 trial program, while undergoing induction chemotherapy, from a total of 88 UK hospitals. Following registration, a tumor sample was tested using next generation sequencing platform for stratification into molecular subtypes including BRAF, PIK3CA, TP53, and RAS mutations (Fig 1 and Data Supplement). Patients were required to provide written informed consent for both tissue testing and entry into any of the randomized subtrials including FOCUS4-C.

Patients were randomly assigned into the FOCUS4-C trial in a subset of 25 hospitals between July 2017 and March 2020. Patients were eligible if their tumor had both RAS and TP53 mutations and they had disease stability or response as assessed by computed tomography (CT) scan at the end of 16 weeks of induction chemotherapy, at which point the chemotherapy ceased and the patient was randomly assigned. Patients required a baseline CT scan 4 weeks before random assignment, a minimum 3-week washout period between the last dose of chemotherapy or biologic therapy and the first dose of adavosertib, adequate renal (creatinine clearance > 50 mL/min) and liver function, a WHO performance status of 0-1, and no evidence of prolonged QT interval on ECG.
**Trial Procedures**

Adavosertib was supplied by AstraZeneca Ltd (Cambridge, UK); packaging, labeling, and distribution were undertaken by Fisher Services (Horsham, UK). Patients randomly assigned to adavosertib continued the drug until disease progression, death, or intolerable toxicity. The first 21 patients received adavosertib 250 mg once daily, on days 1-5 and 8-12 of a 3-week cycle. The next 23 patients received

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**FIG 1.** Flowchart of patients through the trial. CR, complete response; ITT, intention-to-treat; PPA, per-protocol analysis; PR, partial response; SD, stable disease.
adavosertib 300 mg once daily, on the same schedule. Patients took an oral SHT3 antagonist with each dose, and oral dexamethasone 4 mg was given on day 1 and day 8 of each cycle unless clinically contraindicated.

Because of the mandatory supportive medication for nausea and vomiting for which a placebo was not available, binding was not possible, and AM was used as the control arm. Patients randomly assigned to AM followed the same follow-up schedule and remained off any other anticancer treatment until clinical or radiologic evidence of disease progression.

Patient tumor status was assessed at the treating hospital every 8 weeks by CT scan, according to RECIST, version 1.1. Toxicities and symptoms were assessed locally every 4 weeks, using the National Cancer Institute’s Common Terminology Criteria for Adverse Events (version 3.0). Patients remained on trial until disease progression occurred, at which point the patient was recommended to restart the same chemotherapy that was used in the induction phase. Treatment was stopped in the event of grade 3 or worse toxic effects or persistent toxicities judged medically significant or not tolerated by the patient, until the toxicity resolved to grade 1 or better.

Statistical Methods

A full description of the statistical methods is provided in the Data Supplement. In summary, patients were allocated to either adavosertib or AM, using a 2:1 allocation ratio by minimization with a 20% random element. All analyses were performed according to a predefined statistical analysis plan using Stata (version 16.1; Stata Corporation, TX). The primary outcome measure was progression-free survival (PFS), and the prespecified primary efficacy analysis was a per-protocol analysis (PPA) using Cox regression adjusting for minimization factors. Intention-to-treat (ITT) and unadjusted models were also performed as secondary analyses. Sample size calculations were based upon a target hazard ratio (HR) of 0.5 with 80% power and .025 one-sided alpha requiring a target of 26 PFS events in the control arm for final analysis.

RESULTS

Recruitment and Patient Characteristics

The FOCUS4 trial program ran between January 2014 and March 2020. FOCUS4-C ran between April 2017 and March 2020, during which time 817 patients were registered, of whom 718 underwent successful biomarker profiling (Fig 1 and Data Supplement). Two hundred forty-seven patients (34%) had tumors confirmed with both RAS and TP53 mutations (RAS/TP53-mut). Of these, 151 had stable or responding disease after 16 weeks of first-line treatment and 69 were randomly assigned using a 2:1 ratio: 44 to adavosertib and 25 to AM. Of the remaining eligible 82, two chose to be randomly assigned into the concurrent FOCUS4-N trial and others chose not to be randomly assigned into FOCUS4 for reasons such as toxicity from first-line therapy or patient-clinician choice to seek alternative pathways.

Table 1 summarizes the patient baseline characteristics. There were some minor imbalances, which are corrected for in the adjusted analysis (primary model). There were no differences in the frequency of other molecular alterations between the groups. There were no significant differences between the registration period chemotherapy regimens in the adavosertib and AM arms.

Primary Analysis: PFS (per-protocol)

Five patients were excluded from the PPA: four did not start treatment (adavosertib arm) and one was subsequently found to have had progressive disease at the point of random assignment (AM arm). One patient was censored early when they received fluorouracil as anticancer treatment before progression (AM arm).

Within the primary PPA (n = 64), there were 40 of 40 PFS events in the adavosertib arm and 22 of 24 in the AM arm. Patients treated with adavosertib had a longer PFS than those on AM (3.61 vs 1.87 months). Both unadjusted HR (0.52; 95% CI, 0.30 to 0.89; P = .022) and adjusted HR (0.35; 95% CI, 0.18 to 0.68; P = .0022) were statistically significant. Kaplan-Meier curves are provided in Figure 2.

PFS (ITT)

All patients were included in the ITT analysis, but four patients were censored the day after random assignment: three in the adavosertib arm (two because of patient withdrawal and one without any post-random assignment CT scan assessments) and one in the AM arm without any post-random assignment CT scan assessments.

There were 41 of 44 PFS events in the adavosertib arm and 23 of 25 in the AM arm. Consistent with the PPA, the ITT PFS analysis shows a PFS advantage with adavosertib over AM in both the unadjusted (HR = 0.55; 95% CI, 0.32 to 0.94; P = .032) and adjusted analyses (HR = 0.40; 95% CI, 0.21 to 0.75; P = .0051).

Overall Survival (ITT)

There were 27 of 44 deaths in the adavosertib arm and 16 of 25 in the AM arm. There was no significant overall survival (OS) benefit with adavosertib compared with AM (median survival 14.0 vs 12.8 months; unadjusted HR = 0.79; 95% CI, 0.42 to 1.48, P = .47; adjusted HR = 0.92; 95% CI, 0.44 to 1.94, P = .93; Fig 2).

Tumor Control

Adavosertib was associated with a higher proportion of patients with disease control compared with AM (47% vs 28% at any time during the trial), including one patient with a documented partial response to adavosertib (Data Supplement).
patients with a right PTL had no PFS advantage with adavosertib compared with AM (1.87 vs 1.91 months; HR = 1.02; 95% CI, 0.41 to 2.56), whereas those with a left PTL did (3.61 vs 1.87 months, HR = 0.24; 95% CI, 0.11 to 0.51; interaction P = .043; Data Supplement).

This prompted an unplanned subgroup analysis of PTL on OS, and although the numbers of events were low, the interaction was even more marked (Data Supplement). Median OS was 14.1 versus 11.3 months for adavosertib versus AM in left PTL (adjusted HR = 0.37; 95% CI, 0.15 to 0.87) but was 6.5 versus 15.5 months in right PTL (HR = 6.5; 95% CI, 0.72 to 6.43; interaction P = .0032). In terms of response, 38% of right-sided adavosertib patients versus 42% of right-sided AM patients reported disease stability or response at least once while on trial, whereas for left-sided tumors, the figures were 53% versus 19%.

Patients who had responded to induction chemotherapy (v stable disease) and who had two or more metastatic sites appeared to benefit more from adavosertib, albeit to a lesser degree (interaction P value = .14 for response to induction; P = .12 for number of metastatic sites; Fig 3).

External Analyses to Further Characterize the RAS/TP53-Mut Biomarker Population

The RAS/TP53-mutant population has not been previously described. To understand the prognostic implication of this alteration, we analyzed the outcomes of a subset (n = 438) of patients from the FOCUS trial in whom the S:CORT consortium had analyzed a wider panel of CRC genes including KRAS, NRAS, BRAF, MSI, and TP53. The RAS/RAF wild-type group was the reference population (median OS 21.6 months). The RAS/TP53-mutant population is distinct from either mutation alone (RAS or TP53) and had a worse prognosis than either in isolation with a median OS of 14.9 months (HR = 2.06; 95% CI, 1.08 to 3.93; P = .028; Fig 4). This suggests that the RAS/TP53-mut population is a poor-prognosis subgroup but not as marked as for patients with a BRAF mutation or microsatellite instability-high tumor.

These data are consistent with the finding that during the registration period of FOCUS4, 33% of patients in the RAS/TP53-mut population experienced progression during the first 16 weeks of chemotherapy. This is similar to the rate in the BRAF-mutant group (34% progressed) but higher than that seen in RAS-mutant (24%) and all wild-type (22%) subgroups (Data Supplement).

Effect of RAS and TP53 Mutation Subtypes on Adavosertib Activity

We observed that patients with KRAS codon 12/13 mutations had a significant benefit from adavosertib (P for interaction = .014; Fig 3), whereas no detectable benefit was observed in those with KRAS mutations at other codons or with NRAS mutation. Furthermore, the interaction effects of KRAS subtype and of PTL on PFS may be additive as

### TABLE 1. Baseline Patient Characteristics by Randomized Group

| Characteristic                        | Active Monitoring (n = 25) | Adavosertib (n = 44) |
|---------------------------------------|---------------------------|----------------------|
|                                       | Mean (SD) age, years      |                      |
|                                       | 61.9 (12.2)               | 59.2 (12.8)          |
|                                       | No. (%)                   |                      |
|                                       | Male                      | 15 (60)              |
|                                       | Female                    | 10 (40)              |
| Current WHO performance status        |                           |                      |
| 0                                     | 17 (68)                   | 35 (80)              |
| 1                                     | 8 (32)                    | 9 (20)               |
| Site of primary tumor                 |                           |                      |
| Right colon                           | 9 (36)                    | 13 (30)              |
| Left colon                            | 6 (24)                    | 13 (30)              |
| Rectum                                | 10 (40)                   | 18 (41)              |
| Current state of primary tumor        |                           |                      |
| Resected primary                      | 9 (36)                    | 23 (52)              |
| Unresected primary                    | 16 (64)                   | 19 (43)              |
| Unresected local recurrence           | 0 (0)                     | 2 (5)                |
| Timing of metastases                  |                           |                      |
| Metachronous                          | 4 (16)                    | 13 (30)              |
| Synchronous                           | 21 (84)                   | 31 (70)              |
| No. of metastatic sites               |                           |                      |
| One                                   | 6 (24)                    | 16 (36)              |
| Two or more                           | 19 (76)                   | 28 (64)              |
| Disease assessment at end of first-line treatment | | |
| Complete response                     | 0 (0)                     | 1 (2)                |
| Partial response                      | 13 (52)                   | 26 (59)              |
| Stable disease                        | 12 (48)                   | 17 (39)              |
| First-line treatment regimen          |                           |                      |
| FOLFOX                                | 7 (28)                    | 15 (34)              |
| FOLFIRI                               | 8 (32)                    | 14 (32)              |
| CAPOX                                 | 6 (24)                    | 11 (25)              |
| FOLFOXIRI                             | 3 (12)                    | 3 (7)                |
| Others                                | 1 (4)                     | 1 (2)                |
| PIK3CA mutation status                |                           |                      |
| Mutation                              | 1 (4)                     | 1 (2)                |
| Wildtype                              | 24 (96)                   | 43 (98)              |
| Total                                 | 25 (100)                  | 44 (100)             |

Abbreviations: CAPOX, capecitabine and oxaliplatin; FOLFIRI, fluorouracil, leucovorin, and irinotecan; FOLFOX, infusional fluorouracil, leucovorin, and oxaliplatin; FOLFOXIRI, folinic acid, fluorouracil, oxaliplatin, and irinotecan; SD, standard deviation.
there is a significant benefit from adavosertib within the subgroup of left PTL KRAS codon 12/13 subtypes (HR = 0.16; 95% CI, 0.05 to 0.50) and a clear disbenefit within the subgroup of right PTL noncodon 12/13 subtypes (HR = 1.56; 95% CI, 0.49 to 4.97; Data Supplement). The subtype of TP53 mutation or the co-occurrence of PIK3CA mutation did not affect outcome.

Impact of Adavosertib Dosing

As described, during the trial, there was an increase in the dose of adavosertib from 250 mg to 300 mg. PFS was 2.2 months (HR = 0.58; 95% CI, 0.31 to 1.06) with the 250-mg dose and 3.7 months (HR = 0.47; 95% CI, 0.25 to 0.89) with the 300-mg dose; this difference was nonsignificant (P = .48; Data Supplement). Between the 250-mg and 300-mg doses, there was an increased frequency of grade 3 diarrhea (4% v 14%), but otherwise the toxicity profile was similar. There were similar rates of dose modifications between the 250-mg and 300-mg doses: dose delays (16% v 7%), dose reductions (4% v 5%), and dose omissions (19% v 17%). A swimmer plot integrating the effects of adavosertib dose, randomized group, and PTL on PFS is shown in the Data Supplement.

DISCUSSION

Here, we have reported that FOCUS4-C met its primary end point; patients with RAS/TP53-mutant mCRC had PFS advantage with adavosertib compared with AM following induction chemotherapy. These results are particularly encouraging as RAS/TP53-mutant mCRC is a poor prognostic population with limited treatment options. Adavosertib was well-tolerated at both doses evaluated.
The overarching aim of the FOCUS4 trial program was to test novel agents efficiently with specified biomarker subgroups in mCRC with the multi-arm, multi-stage design allowing for an early signal of drug inactivity; thus, any demonstrated efficacy would require further confirmatory study to lead to practice change. FOCUS4-C represents a success of this approach, efficiently demonstrating promising activity of adavosertib within patients with RAS/P53-mutant mCRC, and will directly influence research practice in mCRC.

### Table 1: Subgroup Analyses for PFS by Intention to Treat

| Subgroup                                      | No. of Patients | HR (95% CI)      | P for Interaction |
|-----------------------------------------------|-----------------|------------------|-------------------|
| **Current WHO performance status**            |                 |                  |                   |
| 0                                             | 52              | 0.59 (0.32 to 1.10) | .36               |
| 1                                             | 17              | 0.33 (0.10 to 1.16) |                   |
| **Pre-random assignment disease assessment**  |                 |                  |                   |
| Complete or partial response                   | 39              | 0.31 (0.14 to 0.70) | .14               |
| Stable disease                                 | 30              | 0.63 (0.28 to 1.38) |                   |
| **No. of metastatic sites**                   |                 |                  |                   |
| 1                                             | 22              | 0.84 (0.29 to 2.40) | .12               |
| 2 or more                                     | 47              | 0.35 (0.17 to 0.72) |                   |
| **First-line chemotherapy regimen**           |                 |                  |                   |
| FOLFOX                                         | 22              | 0.33 (0.11 to 0.99) | .67               |
| FOLFIRI                                        | 22              | 0.50 (0.19 to 1.31) |                   |
| CAPOX                                          | 17              | 0.71 (0.23 to 2.16) |                   |
| Others                                         | 8               | 0.21 (0.02 to 1.88) |                   |
| **PIK3CA mutation status**                    |                 |                  |                   |
| Mutation                                       | 9               | 0.75 (0.16 to 3.50) | .35               |
| Wildtype                                       | 60              | 0.37 (0.19 to 0.69) |                   |
| **TP53 mutation subtype**                     |                 |                  |                   |
| Missense                                       | 36              | 0.56 (0.27 to 1.18) | .68               |
| Truncating                                     | 30              | 0.42 (0.17 to 1.02) |                   |
| Neither                                        | 3               | 0.71 (0.04 to 1.79) |                   |
| **KRAS mutation subtype**                     |                 |                  |                   |
| Codons 12 or 13                                | 34              | 0.19 (0.07 to 0.50) | .014              |
| Other KRAS codons or NRAS mutation            | 35              | 0.81 (0.39 to 1.67) |                   |
| **Sidedness of primary tumour (PTL)**         |                 |                  |                   |
| Left-sided                                     | 47              | 0.24 (0.11 to 0.51) | .043              |
| Right-sided                                    | 22              | 1.02 (0.41 to 2.56) |                   |
| **Combination of PTL and KRAS subtype**       |                 |                  |                   |
| Left-sided codons 12 or 13                     | 25              | 0.16 (0.05 to 0.50) | .011              |
| Left-sided other KRAS codons or NRAS mutation | 22              | 0.34 (0.12 to 1.00) |                   |
| Right-sided codons 12 or 13                    | 9               | 0.30 (0.05 to 1.84) |                   |
| Right-sided other KRAS codons or NRAS mutation| 13              | 1.56 (0.49 to 4.97) |                   |
| **Overall (unadjusted)**                      | 69              | 0.52 (0.31 to 0.90) |                   |

**FIG 3.** Subgroup analyses for PFS by intention to treat. CAPOX, capecitabine and oxaliplatin; FOLFIRI, fluorouracil, leucovorin, and irinotecan; FOLFOX, infusional fluorouracil, leucovorin, and oxaliplatin; PFS, progression-free survival; PTL, primary tumor location.
The intermittent treatment strategy used in FOCUS4 follows the demonstration of no detriment in OS in the MRC COIN trial. This is now further substantiated by an individual participant data meta-analysis. Thus, AM is an accepted standard of care following a few months of first-line therapy. FOCUS4 was specifically designed to use this window following first-line induction chemotherapy to test novel agents in specified biomarker groups, before the evolution of multiple resistance mechanisms.

A prespecified analysis demonstrated that adavosertib activity was limited to left colon and rectal PTL, with little activity observed in right PTL. Having observed the significant subgroup effects on PFS, we investigated possible impact on OS. It is provocative to see that in the left-sided tumors, OS was significantly improved with median OS from 11.3 months to 14.1 months (HR = 0.40; 95% CI, 0.17 to 0.97). There is also a possibility of adverse effect on outcome in patients with right PTL. However, the number of patients and events was limited and thus, any conclusions need to be cautious in relation to this observed effect on OS in both subgroups. Differences in CRC by PTL are well-documented, in terms of biology, prognosis, and treatment response, but the mechanisms for differences of treatment efficacy by PTL are not well-understood. An exploratory analysis showed that adavosertib had the most PFS effect in patients with KRAS codons 12/13/TP53-mutant tumors, with lesser activity in those with extended KRAS, or NRAS mutations; functional differences between RAS isoforms are documented. Despite the small sample sizes in FOCUS4-C, the PTL and RAS subtypes subgroup analyses showed interactions significant at the 5% level.
Cumulative reported toxicity, within FOCUS4-C treatment groups and with initial AZD1775 doses separated: (A) active monitoring (n = 50), (B) AZD1775 250 mg (n = 23), and (C) AZD1775 300 mg (n = 21). G, grade; PPE, palmar plantar erythema.

Although these subgroup analyses provide provocative results, we lack a mechanistic explanation for these differences in adavosertib effect; ongoing translational work shall investigate this. We would recommend that further clinical development of adavosertib in the RAS/TP53-mut mCRC population should not be limited by PTL or RAS subtype but should include close monitoring of patients with right PTL and extended RAS mutations to ensure that neither futility nor detriment are observed.

Although the clinical implications of the RAS/TP53 mutation in mCRC are not well-studied, each alteration is individually well-characterized. Here, we have shown that the double RAS/TP53-mutant subgroup carries a moderately poor prognosis (Fig 4) and appears to confer a worse prognosis than either mutation in isolation. This biomarker subgroup has thus shown distinct prognostic and therapeutic relevance and so merits further study in translational work, existing data sets, and ongoing therapeutic trials in mCRC.

Adavosertib has demonstrated an acceptable safety profile; the main toxicity was diarrhea. Efficacy was noted at both the 250-mg and 300-mg doses, with a suggestion of additional activity with the higher dose. We would therefore recommend the 300-mg dosing to progress to further clinical studies in fit patients. However, in the treatment-refractory setting, the 250-mg dose may be more tolerable.

There are limitations to this study. We considered, and would have preferred, a placebo-controlled design; however, at the time of launching FOCUS4-C, high rates of nausea and vomiting had been observed in other adavosertib trials and high-dose steroid antiemetics were considered necessary. For this reason, both clinicians and patient representatives considered a placebo design unfeasible. Given the favorable safety data for single-agent adavosertib in FOCUS4-C, placebo-controlled design could be considered in the future. It is possible therefore that the PFS effect observed was influenced by investigator and patient preference to restart first-line chemotherapy sooner in the AM arm. However, a marked difference in effect was observed between the right and left PTL groups treated with adavosertib, suggesting a lesser effect on the primary analysis because of this potential bias. Additionally, the PFS end point was not centrally reviewed, but assessed in individual sites by RECIST criteria. A further limitation is that by testing adavosertib in the maintenance setting and requiring stability following induction chemotherapy, we have excluded the RAS/TP53 patients with the worse outcome. We therefore cannot generalize the effect of adavosertib within this entire biomarker group.

In conclusion, adavosertib (AZD1775) has demonstrated promising activity compared with AM in patients with RAS/TP53-mut mCRC. This treatment benefit may relate to PTL and KRAS subtype. Given this clear demonstration of efficacy in an RCT and acceptable toxicity profile, future clinical development of adavosertib is warranted particularly as it may represent a future treatment opportunity in this sizable population of unmet need.
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AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO.21.01435.

DATA SHARING STATEMENT

Individual deidentified participant data (including data dictionaries) can be shared upon appropriate application to the MRC CTU at any time from full publication. Study protocols and statistical analysis plan have been provided in the Data Supplement with this manuscript. Going forward, it is proposed that data will be shared with an appropriate international collaborative repository to enable future IPD meta-analysis.

AUTHOR CONTRIBUTIONS

Conception and design: Jenny F. Seligmann, David J. Fisher, Louise C. Brown, Richard A. Adams, Philip Quirke, Timothy C. Humphrey, Mahesh Parmar, Richard Kaplan, Richard Wilson, Matthew Seymour, Timothy S. Maughan

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Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

The full list of FOCUS4 Trial Investigators can be found in Appendix 1.

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Inhibition of WEE1 Is Effective in TP53- and RAS-Mutant Metastatic Colorectal Cancer: A Randomized Trial (FOCUS4-C) Comparing Adavosertib (AZD1775) With Active Monitoring

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO’s conflict of interest policy, please refer to www.asco.org/fwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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No other potential conflicts of interest were reported.
**APPENDIX 1. FULL AUTHORSHIP LIST FOR THE FOCUS4 TRIAL INVESTIGATORS**

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**Trial Steering Committee**
Johnson P. (Chair), Rudd R., Whelan J., and Russell A.

**Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076)**

| Hospital First Name Surname (principal investigator [PI]) |
|----------------------------------------------------------|
| Martin Doak                                              |
| Tamassin Doig                                            |
| Clare Dunbar                                             |
| Ben Elliott                                              |
| Lynne Faragher                                           |
| Paul Fineron                                             |
| Nikki Gilluley                                           |
| Ewa Kondarewicz                                         |
| Jenifer Lauchlan                                         |
| Jim Macpherson                                          |
| Catriona Mclean                                          |
| Hazel Milligan                                           |
| Suzanne Muir                                             |
| Alisa Oswald                                            |
| Ashley Pheely                                            |
| Hamish Phillips                                          |
| Kelly Rust                                               |
| Shaafia Siddiqui                                         |
| Barbara Stanley                                          |
| Moira Stewart                                            |
| Vivienne Wilson                                          |

**St James’s University Hospital (Leeds)**

| Fiona Collinson (PI)                                      |
|-----------------------------------------------------------|
| Matt Seymour                                              |
| Humaira Abbas                                             |
| Ifeoluwa Ajibayo                                          |
| Alan Anthony                                              |
| Hana Ali                                                  |
| Orrie Appell                                              |
| Andrew Barker                                             |
| Vincent Barlow                                            |
| Shana Begum                                               |
| Maxine Berry                                              |
| Judith Chapman                                            |
| Sam Charlton                                              |
| Pam Clark                                                 |
| Emily Rose Crawford                                       |
| Anne Crossley                                             |
| Gemma Dart                                                |
| Jessica Docherty                                          |
| Irina Ershova                                             |
| Alexandra Firth                                          |

(continued in next column)
### Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076) (continued)

| Hospital   | First Name | Surname (principal investigator [PI]) |
|------------|------------|--------------------------------------|
| Jeanifer   | Gachev     |                                      |
| Leanne     | Galloway-Browne |                                |
| Jillian    | Hanson     |                                      |
| Amelie     | Harle      |                                      |
| Farzana    | Haque      |                                      |
| Janine     | Heeley     |                                      |
| Jane       | Hook       |                                      |
| Jane       | Hughes     |                                      |
| Alison     |            |                                      |
| Emma       | Livesey    |                                      |
| Emma       | Lundy      |                                      |
| Michael    | O’Brien    |                                      |
| Mike       | Osborne    |                                      |
| Lauren     | Paul       |                                      |
| Mary       | Perrin     |                                      |
| Annet      | Pillai     |                                      |
| Charlotte  | Richardson |                                   |
| Suzanne    | Rogerson   |                                      |
| Olorunda   | Rotimi     |                                      |
| Emily      | Rudolph    |                                      |
| Jenny      | Seligmann  |                                      |
| Hannah     | Shanks     |                                      |
| Daniel     | Swinson    |                                      |
| Danny      | Ulahannan  |                                      |
| Mariah     | Vorajee    |                                      |
| Sarah      | Wetherop   |                                      |
| Hannah     | Wigginton  |                                      |
| Christopher| Williams   |                                      |
| Jawairiya  | Zubair     |                                      |

### Velindre Hospital

| First Name | Surname (PI) |
|------------|--------------|
| Rob        | Jones        |
| Richard    | Adams        |
| Seema      | Arif         |
| Rebecca    | Bethell      |
| Kathy      | Bishop       |
| Alison     | Brewster     |
| Michael    | Brown        |
| Julie      | Broughton    |
| Lucy       | Chestney     |
| Nikki      | Coates       |
| Sonali     | Dasgupta     |
| Karen      | Davies       |
| Clare      | Donnithorne  |

(continued in next column)

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### Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076) (continued)

| Hospital                     | First Name | Surname (principal investigator [PI]) |
|------------------------------|------------|---------------------------------------|
| Weston Park Hospital         | Joanne     | Hornbuckle (PI)                       |
|                              | Jess       | Aldred                                |
|                              | Cyper      | Allan                                 |
|                              | Richard    | Allen                                 |
|                              | Lynne      | Ashmore                               |
|                              | Darrell    | Barrott                               |
|                              | Alex       | Bradshaw                              |
|                              | Richard    | Brown                                 |
|                              | Sarah      | Brown                                 |
|                              | Kevin      | Chan                                  |
|                              | Rachael    | Clarke                                |
|                              | Su         | Clark                                 |
|                              | Susan      | Clenton                               |
|                              |            | (continued in next column)            |

| Bristol Haematology and Oncology Centre | First Name | Surname (principal investigator [PI]) |
|----------------------------------------|------------|---------------------------------------|
|                                        | Stephen    | Falk (PI)                             |
|                                        |            | (continued on following page)         |
| Hospital            | First Name | Surname (principal investigator [PI]) |
|---------------------|------------|--------------------------------------|
| Kiril               | Delchev    |                                      |
| Kay                 | Drury      |                                      |
| Emily               | Foulstone  |                                      |
| Elysia              | Gower      |                                      |
| John                | Helbrow    |                                      |
| Jon                 | Heywood    |                                      |
| Robert              | Hollister  |                                      |
| Kirsten             | Hopkins    |                                      |
| Hollie              | Jones      |                                      |
| Lauren              | Joyce      |                                      |
| Helen               | Kingston   |                                      |
| Jayne               | Leonard    |                                      |
| Amelia              | Lowe       |                                      |
| Catherine           | McDonald   |                                      |
| Helen               | Monnington |                                      |
| Katarina            | Milutinovic|                                      |
| Jessica             | Nuttall    |                                      |
| Yasmin              | Odding     |                                      |
| Ronak               | Patel      |                                      |
| Ian                 | Penwarden  |                                      |
| Peter               | Robertson  |                                      |
| Tim                 | Robinson   |                                      |
| Sharon              | Short      |                                      |
| Thomas              | Strawson-Smith |                        |
| Kirsty              | Stevenson  |                                      |
| Hannah              | Taylor     |                                      |
| Sandra              | Williams (nee Price) |                |
| Eve                 | Watson     |                                      |
| Axel                | Walther    |                                      |
| Angela              | Webb       |                                      |
| Tom                 | Wilson     |                                      |
| Roland              | Wynn-Williams |                        |
| Royal United Hospital | Emma       | De Winton (PI)                        |
| Louise              | Medley (PI) |                                      |
| Tania               | Allen      |                                      |
| Rowan               | Appleby    |                                      |
| Claire              | Barron     |                                      |
| Leigh               | Biddlestone|                                      |
| Hannah              | Blades     |                                      |
| Ruth                | Brydon-Hill|                                      |
| Shaolin             | Chidavaenzi|                                      |

(continued in next column)

| Hospital            | First Name | Surname (principal investigator [PI]) |
|---------------------|------------|--------------------------------------|
| Ashley              | Cox        |                                      |
| Christine           | Cox        |                                      |
| Claire              | Craig      |                                      |
| Jane                | Crozier    |                                      |
| Samantha            | Curtis     |                                      |
| Michael             | Daly       |                                      |
| Claire              | Dyke       |                                      |
| Rachael             | Exley      |                                      |
| Ioana               | Fodor      |                                      |
| Yuko                | Francis    |                                      |
| Sharath             | Gangadhara |                                      |
| Amy                 | Gaunt      |                                      |
| Jenny               | Gilbert    |                                      |
| Beatrice            | Hamilton   |                                      |
| Leonie              | Harrison   |                                      |
| Carly               | Laxon-Takooree |                          |
| Jill                | MacDonald-Burn |                       |
| Katarzyna           | Machura    |                                      |
| Margaret            | Macmillan  |                                      |
| Carey               | Milson     |                                      |
| Kate                | Moloney    |                                      |
| Sarah               | Murdoch    |                                      |
| Joseph              | Needham    |                                      |
| Abigail             | Pocock     |                                      |
| Vicki               | Portingale |                                      |
| Bryony              | Robertson  |                                      |
| Annie               | Taylor     |                                      |
| Eve                 | Tomlinson  |                                      |
| Tom                 | Tylee      |                                      |
| Rebecca             | Wassall    |                                      |
| Samantha            | Williams   |                                      |
| Jess                | White      |                                      |
| Castle Hill Hospital | Rajarshi   | Roy (PI)                             |
| Abigail             | Alford     |                                      |
| Katie               | Broadbent  |                                      |
| Amandeep            | Dhadda     |                                      |
| Ceri                | Fuller     |                                      |
| Laura               | Hart       |                                      |
| Lyn                 | Harrison   |                                      |
| Joanne              | Hinchcliffe|                                      |
| Linda               | Hoggarth   |                                      |
| Rhian               | Horne      |                                      |
| Dawn                | Jones      |                                      |

(continued on following page)
| Hospital                  | First Name | Surname (principal investigator [PI])  |
|---------------------------|------------|---------------------------------------|
| Victoria Hospital         | Sin        | Lau (PI)                              |
| (Blackpool)               |            |                                       |
|                           | Charlotte  | Armer                                 |
|                           | Denise     | Bennett                               |
|                           | Caroline   | Boardman                              |
|                           | Oliver     | Brennan                               |
|                           | Laura      | Collins                               |
|                           | Falalu     | Danwata                               |
|                           | Alexander Paul | Davies                  |
|                           | Emma       | Davies                                |
|                           | Leanne     | Davies                                |
|                           | Stacey     | Donaldson                             |
|                           | Hannah     | Ferguson                               |
|                           | Amanda     | Finch                                 |
|                           | Julie      | Frudd                                 |
|                           | Karen      | Gratrix                               |
|                           | James      | Haston                                |
|                           | Sue        | Hesketh                               |
|                           | Sue        | Lancaster                             |
|                           | Chris      | Pemberton                              |
|                           | Karen      | Pollard                               |
|                           | Andrew     | Potter                                |
|                           | Jonathan   |                                       |
|                           | Toni       | Purcer                                |
|                           | Ella       | Riedel                                |
|                           | Nicola     | Slawson                               |
|                           | Shabbir    | Susnerwala                            |
|                           | Lauren     | Thornborough                          |
|                           | Conor      | Wilkinson                             |
|                           | Mark       | Wrigley                               |
| Royal Preston Hospital    | Sin        | Lau (PI)                              |
|                           | Amanda     | Alty                                  |
|                           |            | (continued in next column)            |

(continued on following page)
| Hospital                      | First Name | Surname (principal investigator [PI]) |
|-------------------------------|------------|--------------------------------------|
| Hammersmith Hospital          | Harpreet   | Wasan (PI)                            |
| Ilyas                         | Ali        |                                      |
| Nawa                          | Amin       |                                      |
| Gareth                        | Barker     |                                      |
| Michelle                      | Chen       |                                      |
| Sarah                         | Chilcott-Burns |                                  |
| James                         | Clark      |                                      |
| Susan                         | Cleator    |                                      |
| Christopher                   | Coyle      |                                      |
| Andrea                        | Davis-Cook |                                      |
| Keyury                        | Desai      |                                      |
| Matthew                       | Flook      |                                      |
| Victoria                      | Harding    |                                      |
| Gillian                       | Hornzee    |                                      |
| Victoria                      | Latham     |                                      |
| Luzviminda                    | Llemit Ramos |                                  |
| Charles                       | Lowdell    |                                      |
| Maria                         | Martinez   |                                      |
| Daniel                        | Meredith   |                                      |
| Laura                         | Morland    |                                      |
| Annette                       | Musallam   |                                      |
| Chynna                        | Pascual    |                                      |
| Emily                         | Pickford   |                                      |
| David                         | Pinato     |                                      |

(continued in next column)
Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076) (continued)

| Hospital                     | First Name   | Surname (principal investigator [PI]) |
|------------------------------|--------------|--------------------------------------|
| Ethelwolda                   | Goyena       |                                      |
| Andrea                       | Hillyer      |                                      |
| Jane                         | Hosea        |                                      |
| Mohammad                     | Hussain      |                                      |
| Kashif                       | Jarral       |                                      |
| Andrea                       | Jones        |                                      |
| Andrea                       | Kempa        |                                      |
| Adnan                        | Masood       |                                      |
| Craig                        | Macmillan    |                                      |
| James                        | Maloy        |                                      |
| Katherine                    | McGrath      |                                      |
| Jan                          | Miles        |                                      |
| Onyinye                      | Ndefo        |                                      |
| Paula                        | O’Connell    |                                      |
| Malgorzata                   | Polnik       |                                      |
| Ehsan                        | Rahman       |                                      |
| Shahriar Mohammed            | Reza         |                                      |
| Sharon                       | Ryan         |                                      |
| Simon                        | Stapley      |                                      |
| Elizabeth                    | Tee          |                                      |
| Lenka                        | Zvirinska    |                                      |
| Pinderfields Hospital        | Iva          | Damyanova (PI)                       |
| Ashraf                       | Alkhaldi (PI)|                                      |
| Gireesh                      | Kumaran (PI)|                                      |
| Usman                        | Ahmad        |                                      |
| Aneeka Shubnum               | Altaf        |                                      |
| Julie                        | Ball         |                                      |
| Louise                       | Benton       |                                      |
| Kevin                        | Birbeck      |                                      |
| Lynsey                       | Bourner      |                                      |
| Richard                      | Bowers       |                                      |
| Hollie                       | Brooke       |                                      |
| Ellis                        | Burton       |                                      |
| Julie                        | Burton       |                                      |
| Deborah                      | Cooper       |                                      |
| Elizabeth                    | Clayton      |                                      |
| Jane                         | Eastwood     |                                      |
| Aimee                        | Fletcher     |                                      |
| Rebecca                      | Foster       |                                      |
| Darren                       | Gomersall    |                                      |
| Hassan                       | Hameed       |                                      |

(continued in next column)
| Hospital | First Name | Surname (principal investigator [PI]) |
|----------|------------|---------------------------------------|
| Maria Nygren | Shilpa Thapar | Kirsty Ross |
| Patricia Roxburgh | Pavлина Spiliopoulou | Eileen Soulis |
| Kirsteen Stuart | Rasheed Syed | Ashita Waterston |
| Rasheed Syed | Ashita Waterston | Cheryl Wilson |
| Catherine Bale (PI) | Kelly Andrews | Naomi Boyle |
| Claire Fuller | John Grant | Emma Hall |
| Anna Mullard | Wendy Saxton | Nick Stuart |
| Alice Thomas | Linzi Williams | Rachel Williams |
| Sarah Gwynne (PI) | Fay Annison | Sharon Armstrong |
| Michael Christie | Kay Campbell | Angie Cheyne |
| Kathryn Connolly | Pat Cooper | Amber Johnson |
| Susan Martin | Celia Meneses | Graeme Murray |
| Nicola Price | Sue Rodwell | Mhairi Scott |
| Margaret Smith | Bartosz Was | Mehmoood Zaidi |
| Ishtiaq Zubairi | Cheltenham General Hospital | Kim Berstein (PI) |
| Moe (PI) | Rehana Bakawala | Sarah Beazer |
| Anikat | Colin Binks | Lucy Blake |
| Asande | Sarah Beazer | Colin Binks |
| Evans | Lucy Blake | Bethan Cartwright |
| Garrard | Samuel Croly | Lin Crossley |
| Griffiths | Rachel Durrant | Rachel Durrant |
| Hughes | David Farrugia | Janet Forkes |
| MacPhee | Emma Gilbert | Fabrizio Mauri |
| Murphy | Elaine Pratten | Nick Reed |
| Pope | Elizabeth Read | Rachel Sayers |
| Riba | Shilpa Thapar | Lesley Shepherd |
| Rolls | Shilpa Thapar | Neil Shepherd |
| Taylor | Shilpa Thapar | Stephen Shepherd |

(continued in next column)
| Hospital                                    | First Name | Surname (principal investigator [PI]) |
|--------------------------------------------|------------|--------------------------------------|
| Clatterbridge Centre for Oncology          | Nasim      | Ali (PI)                             |
| Wesley Artiste                             |            |                                      |
| Shaker Abdallah                            |            |                                      |
| Alexandra Bailey                           |            |                                      |
| Danielle Campbell                          |            |                                      |
| Maggie Cantrell                            |            |                                      |
| Joanne Cliff (nee Mooney)                  |            |                                      |
| Thomas Davies                              |            |                                      |
| Helen Flint                                |            |                                      |
| Amy Ford                                   |            |                                      |
| Barbara King                               |            |                                      |
| Ayman Madi                                 |            |                                      |
| Samah Massalha                             |            |                                      |
| Laura McAllister                           |            |                                      |
| Amir Montazeri                             |            |                                      |
| Joanne Mullen                              |            |                                      |
| Julie O'Hagan                              |            |                                      |
| Anna Olsson-Brown                          |            |                                      |
| Katharine Pelton                           |            |                                      |
| Kelly Richardson                           |            |                                      |
| Sandra Robinson                            |            |                                      |
| Joseph Sacco                               |            |                                      |
| Sarah Stuart                               |            |                                      |
| Hollie Wilson                              |            |                                      |
| Perme Yesildag                             |            |                                      |
| Mariah Zavery                              |            |                                      |
| Royal Devon and Exeter Hospital            | Melanie    | Osborne (PI)                         |
| Kizzy Baines                               |            |                                      |
| Tamika Chapter                             |            |                                      |
| Elizabeth Davey                            |            |                                      |
| Susan Downer                               |            |                                      |
| Dawn Edwards                               |            |                                      |
| Theresa Lawless                            |            |                                      |
| James Leavy                                |            |                                      |
| Mark Napier                                |            |                                      |

(continued in next column)
### Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076) (continued)

| Hospital             | First Name | Surname (principal investigator [PI]) |
|----------------------|------------|---------------------------------------|
| Rosina               | Donovan    |                                       |
| Lola                 | Enemuwe    |                                       |
| Victor               | Eneh       |                                       |
| Gabrielle            | Gould      |                                       |
| Todd                 | Gumbleton  |                                       |
| Selina               | Gurung     |                                       |
| Gemma                | Hector     |                                       |
| Sonya                | Hessey     |                                       |
| Daniel               | Hochhauser |                                       |
| Sabrina              | Holohan    |                                       |
| Michelle             | Hung       |                                       |
| Georgios             | Imseeh     |                                       |
| Adoracion            | Jayme      |                                       |
| Sarah                | Kerr       |                                       |
| Khurum               | Khan       |                                       |
| Jennifer             | Laude      |                                       |
| Xiao                 | Lu         |                                       |
| Gina                 | Margai     |                                       |
| Katie                | Matthews   |                                       |
| Eman                 | Mohamad    |                                       |
| Fatima               | Mohamed    |                                       |
| Sam                  | Morris     |                                       |
| Anna                 | Nikopoulou |                                       |
| Mayur                | Patel      |                                       |
| Maria                | Power      |                                       |
| Prakash              | Rao        |                                       |
| Manuel               | Rodriguez-Justo |                    |
| Derya                | Sahin      |                                       |
| Kai Keen             | Shiu       |                                       |
| Luke Owen            | Steventon  |                                       |
| Mark                 | Sunga      |                                       |
| Hinesh               | Tailor     |                                       |
| Anisa                | Tariq      |                                       |
| Varji                | Thayalan   |                                       |
| Jennifer             | Thomas     |                                       |
| Christopher          | Wanstall   |                                       |
| Kristian             | Warnes     |                                       |
| Christopher          | Whilton    |                                       |
| Georgina             | Wood       |                                       |
| Lisa                 | Rogers     | (Monklands Hospital, PI)              |
| Anne                 | McKilop    | (Monklands Hospital, PI)              |
| Ashita               | Waterston  | (Monklands Hospital, PI)              |

(continued in next column)
Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076) (continued)

| Hospital                        | First Name | Surname (principal investigator [PI]) |
|---------------------------------|------------|---------------------------------------|
| Churchill Hospital, Oxford      | Tim        | Maughan (PI)                          |
|                                 | David      | Badcock                               |
|                                 | Magdalena  | Benysek                               |
|                                 | Rosita     | Broderick                             |
|                                 | Anne       | Butterfield                           |
|                                 | Evelyn     | Chan                                  |
|                                 | Philip     | Charlton                              |
|                                 | David      | Church                                |
|                                 | Richard    | Cousins                               |
|                                 | Louise     | Cowen                                 |
|                                 | Joanne     | Davies                                |
|                                 | Steven     | Davis                                 |
|                                 | Alfonso    | Gonzalez Blas                         |
|                                 | Will       | Goodman                               |
|                                 | Nikki      | Hayward                               |
|                                 | Clare      | Jacobs                                |
|                                 | Patrycja   | Jastrzebska                           |
|                                 | Evanthia   | Komminidou                            |
|                                 | Jonathan   | Lau                                   |
|                                 | Carolina   | Lepiato                               |
|                                 | Clare      | Marken                                |
|                                 | Kerrie     | Marston                               |
|                                 | Mark       | Middleton                             |
|                                 | Ann        | Murphy                                |
|                                 | Rebecca    | Muirhead                              |
|                                 | Adrian     | Nicholson                             |
|                                 | Robin      | Peach-Toon                            |
|                                 | Navin      | Pol                                   |
|                                 | Sally      | Rich                                  |
|                                 | Nicola     | Stoner                                |
|                                 | James      | Wakelin                               |

(continued in next column)
| Hospital | First Name | Surname (principal investigator [PI]) |
| --- | --- | --- |
| Victoria Hospital (Kirkcaldy) | Sally | Clive (PI) |
| | Brian | Adamson |
| | Julie | Aitken |
| | John | Brush |
| | Rebecca | Cain |
| | Lesley | Cargill |
| | Shona | Cheyne |
| | Clare | Cliff |
| | Hazel | Cree |
| | Karen | Gray |
| | Sophie | Iwanikw |
| | Fiona | Johnston |
| | Alastair | Matthews |
| | Wendy | McCorry |
| | Catriona | Mclean |
| | Fiona | Murdoch |
| | Ibrahim | Nawroz |
| | Julie | Penman |
| | Anna | Scott |
| | Maria | Simpson |
| | Deepak | Subedi |
| | Jennifer | Tait |

(continued in next column)

| Hospital | First Name | Surname (principal investigator [PI]) |
| --- | --- | --- |
| | Michelle | Tingley |
| | Linzi | Wilson |
| Princess Alexandra Hospital (Harlow) | John | Bridgewater (PI) |
| | Gemma | Cook |
| | Amelia | Daniel |
| | Venkatesh | Gajapathy |
| | Evelyn | Holmes |
| | Tayo | Jayesimi |
| | Joanne | Kellaway |
| | Teresa | Light |
| | Lucinda | Melcher |
| | Cait | Rees |
| | Vasi | Sundaresan |
| Royal Surrey County Hospital | Tony | Dhillon (PI) |
| | Mazhar | Ajaz |
| | Nawa | Amin |
| | Humyraa | Aziz |
| | Izhar | Bagwan |
| | Catherine | Blake |
| | Fiona | Butler |
| | Penny | Champion |
| | Karen | Chan |
| | Sebastian | Cummins |
| | Tineke | Edmunds |
| | Sharadah | Essapen |
| | Andrew | Furness |
| | Laura | Gordon |
| | Di | Grainger |
| | Helen | Graves |
| | Imogen | Heenan |
| | Kirsty | Horwood |
| | Daniel | Jennings |
| | Natasha | Kamboh |
| | Aga | Kehinde |
| | Karla | Lee |
| | Sibylle | Lintott |
| | Gaybrielle | Livingstone |
| | Cheryl | Marriott |
| | Catherine | Medcalf |
| | Aruna | Medisetti |
| | Mahomed | Moosa |

(continued on following page)
| Hospital                        | First Name | Surname (principal investigator [PI]) |
|--------------------------------|------------|---------------------------------------|
| Gayathri Nagarajan             |            |                                       |
| Sarah Oakes                    |            |                                       |
| Sue Sargent                    |            |                                       |
| Alexandra Stewart              |            |                                       |
| Hasina Thandar                 |            |                                       |
| Claire Thompson                |            |                                       |
| Katharine Webb                 |            |                                       |
| Rosalyne Westley               |            |                                       |
| Julia Whittle                  |            |                                       |
| Julie Wilkinson                |            |                                       |
| Rebecca Wills                  |            |                                       |
| St Helens Hospital             | Zahed      | Khan (PI)                             |
| Rachel Cassidy                 |            |                                       |
| Jenny Cotton                   |            |                                       |
| Lisa Dobson                    |            |                                       |
| Nicola Hornby                  |            |                                       |
| Sheila Kelly                   |            |                                       |
| Amanda McCairsty               |            |                                       |
| Jeanette Ribton                |            |                                       |
| Michelle Robinson              |            |                                       |
| Carol Ross                     |            |                                       |
| Victoria Thomas                |            |                                       |
| Chesterfield Royal Hospital    | Vanessa    | Wilshaw (PI)                          |
| Ibrahim Al-Modaris             |            |                                       |
| Rebecca Clark                  |            |                                       |
| Aurora Del Pozo                |            |                                       |
| Alice Dewdyney                 |            |                                       |
| Nicky Ford                     |            |                                       |
| Rachel Gascoyne                |            |                                       |
| Neeta Gogna                    |            |                                       |
| Charlotte Hoult                |            |                                       |
| Emma Hudson                    |            |                                       |
| Kelly Pritchard                |            |                                       |
| Martin Shepherd                |            |                                       |
| Lesley Stevenson               |            |                                       |
| Danesh Taraporewalla          |            |                                       |
| Julie Toms                     |            |                                       |
| Katie Wallace                  |            |                                       |
| Julie Whitehead                |            |                                       |
| Lucinda Wilson                 |            |                                       |
| Ipswich Hospital               | Gopalakrishnan Srivivasan (PI) | |
| Zoltan Szucs (PI)              |            |                                       |

(continued in next column)
| Hospital                   | First Name | Surname (principal investigator [PI]) |
|---------------------------|------------|--------------------------------------|
| Calderdale Royal Hospital | Jo         | Dent (PI)                            |
|                           | Mohammad   | Irfan                                |
|                           | Nick       | Brown                                |
|                           | Nicky      | Daker                                |
|                           | Sam        | Dale                                 |
|                           | Denise     | Hancock                              |
|                           | James      | Harris                               |
|                           | Lisa       | Horner                               |
|                           | Jeremy     | Hyde                                 |
|                           | Rebecca    | Jenkins                              |
|                           | Christopher| Knight                               |
|                           | Mandy      | Madigan                              |
|                           | Adam       | Mawer                                |
|                           | Belinda    | McLean                               |
|                           | Sabiha     | Ravat                                |
|                           | Hannah     | Riley                                |
|                           | Jodie      | Rowan                                |
|                           | Simone     | Deborah                              |
|                           | Lisa       | Deborah                              |
|                           | Selina     | Shaw                                 |
|                           | Kathryn    | Smith                                |
|                           | Christine  | Turner                               |
|                           | Georgina   | Turner                               |
|                           | Hayley     | Webster                              |
|                           | Tracy      | Wood                                 |
| Derriford Hospital        | David      | Sherriff (PI)                        |
|                           | Rebecca    | Aaron                                |
|                           | Bridget    | Aire                                 |
|                           | Baffour    | Amo-Takyi                            |
|                           | Erin       | Brennan                              |
|                           | Lucy       | Cadmore                              |
|                           | Leonie     | Eastlake                             |
|                           | Laura      | Evenden                              |
|                           | Kay        | Facey                                |
|                           | Olivia     | Fraser                               |
|                           |            | (continued in next column)           |

Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076) (continued)
| Hospital             | First Name | Surname (principal investigator [PI]) |
|----------------------|------------|--------------------------------------|
| Addenbrooke’s Hospital | Hugo      | Ford (PI)                            |
|                      | Athar      | Ahmad                                |
|                      | Alexandra  | Azevedo                              |
|                      | Lesley     | Bennett                              |
|                      | Elizabeth  | Blake                                |
|                      | Mark       | Bolton                               |
|                      | Rebecca    | Bradley                              |
|                      | Jane       | Bushen                               |
|                      | Joanna     | Calder                               |
|                      | Anita      | Chhabra                              |
|                      | Kathy      | Chin                                 |
| (continued in next column) |           |                                       |

| Hospital             | First Name | Surname (principal investigator [PI]) |
|----------------------|------------|--------------------------------------|
|                      | Sarah      | Clark                                |
|                      | Joseph     | Gallagher                            |
|                      | Svitlana   | Iyevkova                             |
|                      | Rashmi     | Jadon                                |
|                      | Catherine  | Jephcott                             |
|                      | Natalie    | Jones                                |
|                      | Hannah     | Loveday                              |
|                      | Jane       | Macdonald                            |
|                      | Betania    | Mahler-Araujo                        |
|                      | Debra      | Mansengh                             |
|                      | Ultan      | McDermott                            |
|                      | Lindsay    | Piper                                |
|                      | Amy        | Strong                               |
|                      | Catherine  | Thorbinson                           |
|                      | Saji       | Victor                               |
|                      | Naval      | Vyse                                 |
|                      | Amanda     | Walker                               |
|                      | Emma       | Wong                                 |
|                      | Zsuzsa     | Zaborszky                            |
| (continued on following page) |           |                                       |

Guy’s Hospital (London) | Paul | Ross (PI) |
|------------------------|------|-----------|
| Samantha               | Barrett |
| Eva                    | Batovska |
| Jessica                | Brady    |
| Maribel                | Boyce    |
| Laura                  | Camburn  |
| Lorna                  | Caplis   |
| Noan Minh              | Chall    |
| Jason                  | Chow     |
| Chi Yee                | Chung    |
| Sophie                 | Clark    |
| Sarah                  | Cleary   |
| Victoria               | Donovan  |
| Sandra                 | Esteban Moreno |
| Adrienn                | Fazekasne Fulep |
| Lucy                   | Featherstone |
| Michael                | Flanagan |
| Laura                  | Green    |
| Sara                   | Hulf     |
| Arun                   | Karnad   |
| Sara                   | Kazemzadeh |
| Vevangaune             | Ketjiperue |
| (continued on following page) |      |           |
| Hospital                      | First Name          | Surname (principal investigator [PI]) |
|-------------------------------|---------------------|---------------------------------------|
| St George’s Hospital (London)| Fiona               | Lofts (PI)                            |
|                               | Doraid              | Alrifa                                |
|                               | Nia                 | Alsamarrai                            |
|                               | Jason               | Chow                                  |
|                               | Alice               | Dainty                                |
|                               | Lorette             | Ffolkes                               |
|                               | Caroline            | Finlayson                              |
|                               | Claire              | Gilmartin                              |
|                               | Anne                | Haldeos                               |
|                               | Sam                 | Hollingworth                           |
|                               | Geoffrey            | Howell                                |
|                               | Robert              | Ingham                                |
|                               | Kay                 | Laurent                               |
|                               | Vitalis             | Nwokorie                               |
|                               | Antonio             | Pesino                                |
|                               | Mark                | Quarrell                              |
|                               | Agne                | Sekmokaite                             |
|                               | Jesusa              | Toledo                                |
| Wrexham Maelor Hospital       | Simon               | Gollins (PI)                          |
|                               | Stacy               | Ackerley                              |
|                               | Ashraf              | Alkhaledi                             |
|                               | Kelly               | Andrews                               |
|                               | Rachel              | Davies                                |

(continued in next column)
| Hospital                  | First Name | Surname (principal investigator [PI]) |
|---------------------------|------------|--------------------------------------|
| James Cook University Hospital | Nick       | Wadd (PI)                            |
|                           | Andrea     | Boyce                                |
|                           | Alison     | Chivers                              |
|                           | Anthony    | Donnelly                             |
|                           | Helen      | Dunn                                 |
|                           | Vicky      | Hanlon                               |
|                           | Charlotte  | Jacobs                               |
|                           | Steven     | Liggett                              |
|                           | Craig      | Mower                                |
|                           | Lisa       | Peacock                              |
|                           | Jacqueline | Richards                             |
|                           | Agnieszka  | Skotnicka                            |
|                           | Danielle   | Sweeney                              |
|                           | Jane       | Thompson                             |
|                           | Hans       | Van der Voet                         |
|                           | Gill       | Wheater                              |
|                           | David      | Wilson                               |
|                           | Jason      | Wong                                 |
| Poole Hospital            | Amelie     | Harle (PI)                           |
|                           | Tamas      | Hickish (PI)                         |
|                           | Michael    | Adrio                                |
|                           | Maria      | Alban                                |
|                           | Julian     | Alexander                            |
|                           | Lyn        | Allen                                |
|                           | Mary       | Apps                                 |
|                           | Beth       | Aubrey                               |
|                           | Helen      | Bradley                              |
|                           | Savina     | Eloitva                              |
|                           | Daniel     | Fielding                             |
|                           | Maxine     | Flubacher                            |
|                           | Deborah    | Forster                              |
|                           | Melanie    | Foster                               |
|                           | Louise     | Heckford                             |
|                           | Jill       | Hobson                               |
|                           | Hannah     | James                                |
|                           | Min Yee    | Lee                                  |
|                           | Helen      | Morling                              |
|                           | Victoria   | Osborne                              |
|                           | Sharon     | Power                                |
| Royal Cornwall Hospital   | Richard    | Ellis (PI)                           |
|                           | Linda      | Allsop                               |
|                           | Nicholas   | Ashley                               |
|                           | Kerry      | Atkinson                             |
|                           | Nigel      | Bailey                               |
|                           | Thea       | Barlow                               |
|                           | Kayleigh   | Bennett                              |
|                           | Carolyn    | Brode                                |
|                           | Thomas     | Cornell                              |
|                           | Alexander  | Dengler                              |
|                           | Emma       | Duley                                |
|                           | Sophia     | Eloi                                 |
|                           | Caroline   | Goddard                              |
|                           | Aaron      | Gould                                |
|                           | Anne       | Griffiths                            |
|                           | Karina     | Harris                               |
|                           | Peter      | Hellwell                             |
|                           | Claire     | Hill                                 |
|                           | Louise     | Johns                                |
|                           | Tinnaya    | King                                 |
|                           | Samantha   | Lomax                                |
|                           | Kirsty     | Maclean                              |
|                           | John       | Madine                               |
|                           | Joe        | Mathew                               |
|                           | John       | McGrane                              |
|                           | Fiona      | Minear                               |
|                           | Sharon     | Moore                                |
|                           | Anna       | Oakes                                |
|                           | Caroline   | Parnell                              |
|                           | Kerenia    | Partridge                            |
|                           | Sallyanne  | Platt                                |
|                           | Kirsty     | Prout                                |
|                           | William    | Pynsent                              |
|                           | Rebecca    | Rogers                               |
|                           | Jenifer    | Row                                  |
|                           | Laura      | Royle                                |
|                           | Johanna    | Skewes                               |
|                           | Victoria   | True                                 |
|                           | Craig      | Vincent                              |
|                           | Roger      | Wheelwright                          |
| (continued in next column) |           | (continued in next column)          |

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Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076) (continued)

| Hospital                        | First Name | Surname (principal investigator [PI]) |
|---------------------------------|------------|--------------------------------------|
| South Tyneside District Hospital| Ashraf     | Azzabi (PI)                          |
|                                 | Amy        | Burns                                |
|                                 | Kumud      | Jain                                 |
|                                 | Judith     | Moore                                |
|                                 | Ruth       | Tindle                               |
| St Bartholomew's Hospital       | David      | Propper (PI)                         |
| (London)                        | Waheeda    | Abida                                |
|                                 | Hayley     | Blackgrove                           |
|                                 | Joanne     | Chin-Aleong                          |
|                                 | Nikolaos   | Diamantis                            |
|                                 | Resmi      | Jayachandran                         |
|                                 | Sumaiya    | Kamora                               |
|                                 | Cheryl     | Lawrence                             |
|                                 | Alia       | Mahboob                              |
|                                 | Juan       | Navarro                              |
|                                 | Tanjil     | Nawaz                                |
|                                 | Pratisha   | Panday                               |
|                                 | Hannah     | Payne                                |
|                                 | Stephen    | Russell                              |
|                                 | Sarah      | Slater                               |
| Yeovil District Hospital        | Andrew     | Allison (PI)                         |
|                                 | Erica      | Beaumont (PI)                        |
|                                 | Matthew    | Sephton (PI)                         |
|                                 | Joanna     | Allison                              |
|                                 | Zenaida    | Armstrong                            |
|                                 | Claire     | Barron                               |
|                                 | Nigel      | Beer                                 |
|                                 | Kate       | Beesley                              |

(continued in next column)

| Hospital                        | First Name | Surname (principal investigator [PI]) |
|---------------------------------|------------|--------------------------------------|
|                                 | Edwin      | Cooper                               |
|                                 | Sarah      | De Bruijn                            |
|                                 | David      | Donaldson                            |
|                                 | Tracey     | Duckett                              |
|                                 | Adam       | Edwards                              |
|                                 | Shirley    | Fox                                  |
|                                 | Karen      | Flynn                                |
|                                 | Michelle   | Kotze                                |
|                                 | Michaela   | Nock                                 |
|                                 | Jess       | Perry                                |
|                                 | Lucy       | Pippard                              |
|                                 | Kerry      | Rennie                               |
|                                 | Amber      | Rowsell                              |
|                                 | Rufus      | Smith                                |
|                                 | Lesley     | Thomas                               |
|                                 | Barbara    | Williams-Yesson                       |
| Lincoln County Hospital         | Zuzana     | Stokes (PI)                          |
|                                 | Antoinette | Adu                                  |
|                                 | Suzanne    | Archer                               |
|                                 | Sarah      | Bell                                 |
|                                 | Jayne      | Borley                               |
|                                 | Sarah      | Coombs                               |
|                                 | Olesya     | Francis                              |
|                                 | Annette    | Hildrith                             |
|                                 | Kathryn    | Hoare                                |
|                                 | Carol      | Lockwood                             |
|                                 | Maryanne   | Okubanjo                             |
|                                 | Rhiannan   | Pegg                                 |
|                                 | Manuel     | Ruiz-Echarri                         |
|                                 | Thomas     | Sheehan                              |
|                                 | Anuradha   | Sheth                                |
|                                 | Andrew     | Sloan                                |
|                                 | Caroline   | Taylor                               |
|                                 | Ruth       | Thoy                                 |
|                                 | Alyson     | Wilson                               |
| Maidstone Hospital              | Mark       | Hill (PI)                            |
|                                 | Doraid     | Airifa                               |
|                                 | Elizabeth  | Angus                                |
|                                 | Paulette   | Basham                               |
|                                 | Lisa       | Brown                                |
|                                 | Tracey     | Chambers                             |
|                                 | Alison     | Davison                              |

(continued on following page)
| Hospital                          | First Name | Surname (principal investigator [PI]) |
|-----------------------------------|------------|--------------------------------------|
| Jackie Evans                      |            |                                      |
| Sanjina Kathuria                  |            |                                      |
| Samantha Kestenbaum               |            |                                      |
| Tiana Kordbacheh                  |            |                                      |
| Satish Kumar                      |            |                                      |
| Barbara LeBrocq                   |            |                                      |
| Gemma McCormick                   |            |                                      |
| Christos Mikropoulos              |            |                                      |
| Ian Pamphlett                     |            |                                      |
| Joanne Patterson                  |            |                                      |
| Caroline Rodger                   |            |                                      |
| Holly Slater                      |            |                                      |
| Charlotte Stevens                 |            |                                      |
| Jeff Summers                      |            |                                      |
| Alicia Synowiec                   |            |                                      |
| Katy Taylor                       |            |                                      |
| Lisa Tribe                        |            |                                      |
| Cristina Lopez Escola (PI)        |            |                                      |
| Rebecca Ashton                    |            |                                      |
| Suha Atabani                      |            |                                      |
| Alex Blades                       |            |                                      |
| Emma Blades                       |            |                                      |
| Lauren Blackburn                  |            |                                      |
| Pauline Brookes                   |            |                                      |
| Eliot Chadwick                    |            |                                      |
| Caroline Coulson                  |            |                                      |
| Michelle Cunnell                  |            |                                      |
| James Donworth                    |            |                                      |
| Jade Eggleton                     |            |                                      |
| Susan Elliott                     |            |                                      |
| Joanne Hobbs                      |            |                                      |
| Shaymaa Hosni                     |            |                                      |
| Laura Kirk                         |            |                                      |
| Emma Marshall                     |            |                                      |
| Balwir Matharoo-Ball              |            |                                      |
| Kayleigh Mills                    |            |                                      |
| Jamie Mills                       |            |                                      |
| Jeanette Mulhurn                  |            |                                      |
| Karen Newcombe                    |            |                                      |
| Vanessa Potter                    |            |                                      |
| Tin Sang-Tsang                    |            |                                      |

(continued in next column)
| Hospital                  | First Name | Surname (principal investigator [PI]) |
|---------------------------|------------|--------------------------------------|
| Weston General Hospital   | Stephen    | Falk (PI)                            |
|                           | Paola      | Di Nardo (PI)                        |
|                           | Marjorie   | Tomlinson                            |
|                           | Kathy      | Beard                                |
|                           | Sandra     | Beech                                |
|                           | Hannah     | Berry                                |
|                           | Debbie     | Coles                                |
|                           | Donna      | Cotterill                            |
|                           | Harvey     | Dymond                               |
|                           | Symeon     | Eleftheriadis                         |
|                           | Rajesh     | Gamare                               |
|                           | Christine  | Graham                               |
|                           | Serena     | Hilman                               |
|                           | Sarah      | Kidd                                 |
|                           | Denise     | Leighton-Price                        |
|                           | Hugh       | Lloyd-Jones                           |
|                           | Andrew     | McKendrick                            |
|                           | Kathryn    | Munday                               |
|                           | Vivienne   | Pixton                                |
|                           | Glenn      | Saunders                             |
|                           | Ed         | Sheffield                             |
|                           | Dawn       | Simmons                              |
|                           | Axel       | Walther                               |
|                           | Rachel     | Warinton                             |
|                           | Tom        | Wells                                |
| Glangwili General Hospital| Mau-Don    | Phan (PI)                             |
|                           | Samantha   | Coetzee                               |

(continued in next column)

| Hospital                  | First Name | Surname (principal investigator [PI]) |
|---------------------------|------------|--------------------------------------|
| Royal Albert Edward Infirmary | Francisca Marti | Marti (PI)                        |
|                           | Elena      | Takeuchi (PI)                        |
|                           | Jennifer   | Cannon                               |
|                           | Kate       | Chilman                              |
|                           | Shien      | Chow                                 |
|                           | Louise     | Devereaux                            |
|                           | Alison     | Doran                                |
|                           | Diane      | Forrest                              |
|                           | Karen      | Moss                                 |
|                           | Monica     | Patel                                |
|                           | Angela     | Power                                |
|                           | Wendy      | Stevens                              |

(continued on following page)
| Hospital                          | First Name | Surname (principal investigator [PI]) |
|----------------------------------|------------|---------------------------------------|
| Victoria Corner                  | Abigail    | Edwards                               |
| Adrienn                          | Angela     | Frith                                 |
| Julie                            | Liz        | Happle                                |
| Roger                            | Andrew     | Jackson                               |
| Lauriane Kernwood                | Lauriane   | Kerwood                               |
| Kathryn                          | Emma       | Magras                                |
| Asmat                            | Christina  | Narh                                  |
| Pennie                           | Arun       | Selvaraju                             |
| Jackie                           | Claire     | Williams                              |
| Dawn Storey (PI)                 | Joanne     | Blackburn                             |
| Stephanie Brogan                 | Raj        | Burgul                                |
| Eilidh Henderson                 | Jane       | Keddie                                |
| Linnet McGeever                  | Kaye       | McIlvar                               |
| David McIntosh                   | Caroline   | Mcleary                               |
| Lynn McGeever                    | Annette    | Riley                                 |
| Joanne Robinson                  | Anne       | Todd                                  |
| Patricia Turner                  | Sally      | Young                                 |
| Mark Harrison (PI)               | Farhan     | Ahmed                                 |
| Nicola Anyamene                  | Nicky      | Barnes                                |
| Neel Bhuva                       | Sam        | Bosompem                              |
| Kari Evans                       |            | (continued in next column)            |
| Forth Valley Royal Hospital      |            | (continued in next column)            |
| Mount Vernon Hospital            |            | (continued in next column)            |
| Queen Elizabeth Hospital (Birmingham) | Gary      | Middleton (PI)                        |
| Queen’s Hospital Burton          | Manjusha   | Keni (PI)                             |
|                                  |            | (continued on following page)         |

WEE1 Inhibition in Metastatic Colorectal Cancer
| Hospital                      | First Name | Surname (principal investigator [PI]) |
|------------------------------|------------|--------------------------------------|
| Russells Hall Hospital       | Ankit      | Jain (PI)                            |
| Simon                        | Grumett    | (PI)                                 |
| Joann                        | Atkinson   |                                      |
| Daniel                       | Bull       |                                      |
| Donna                        | Cleal      |                                      |
| Lesley                       | Edwards    |                                      |
| Kath                         | Harrow     |                                      |
| Stacey                       | Jennings   |                                      |
| Lucy                         | Kadiki     |                                      |
| Karen                        | Kanyi      |                                      |
| Sally                        | Keates-Porter |                                |
| Pek                          | Keng-Koh   |                                      |
| Margaret                     | Marriott   |                                      |
| Julie                        | Matthews   |                                      |
| Karen                        | McGarry    |                                      |
| Vanessa                      | Moore      |                                      |
| Andrew                       | Moore      |                                      |
| Manesh                       | Patel      |                                      |
| Veena                        | Shinde     |                                      |
| Lucie                        | Smith      |                                      |
| Lucy                         | Smith      |                                      |
| Angela                       | Watts      |                                      |
| Singleton Hospital           | Sarah      | Gwynne (PI)                          |
| Cristina                     | Lopez      | (PI)                                 |
| Alya                         | Al-Affan   |                                      |
| Philip                       | Bryant     |                                      |
| Karen                        | Chesters   |                                      |
| Sharon                       | Davies     |                                      |
| Jenna                        | Edwards    |                                      |
| Stuart                       | Evans      |                                      |
| Tracey                       | Ford       |                                      |
| Ricky                        | Frazer     |                                      |
| Judith                       | Gooding    |                                      |
| Olivia                       | Hatcher    |                                      |
| Gillian                      | Jones      |                                      |
| Lewis                        | Jones      |                                      |
| Maung                        | Moe        |                                      |
| Karen                        | Phillips   |                                      |
| Euan                         | Pratt      |                                      |
| Alex                         | Richards   |                                      |
| Louise                       | Thomas     |                                      |
| University Hospital Coventry | Vanessa    | Potter (PI)                          |
| Julie                        | Turner     |                                      |
| Nia                          | Viney      |                                      |
| Dawn                         | Withers    |                                      |
| University Hospital of North Tees | Madhavi    | Adusumalli (PI)                    |
| David                        | Wilson     | (PI)                                 |
| Alison                       | Chilvers   |                                      |
| Helen                        | Dunn       |                                      |
| Sarah                        | Essex      |                                      |
| Mohammad                     | Hegab      |                                      |
| Hyder                        | Latif      |                                      |
| Moira                        | Percival   |                                      |
| Sarah                        | Pitcairn   |                                      |
| Lynda                        | Poole      |                                      |
| Pam                          | Race       |                                      |

(continued in next column)
| Hospital                       | First Name | Surname (principal investigator [PI]) |
|-------------------------------|------------|---------------------------------------|
| Whittington Hospital (London) | Pauline    | Leonard (PI)                          |
|                               | Rashidat   | Adeniba                               |
|                               | Dhili      | Arul                                  |
|                               | Jonathan   | Flor                                  |
|                               | Kavita     | Kantilal                              |
|                               | Xiao Lou   | Lu                                    |
|                               | Mulyati    | Mohamed                               |
|                               | Michelle   | Sauli                                 |
|                               | Nuray      | Temiz                                 |
|                               | Azmina     | Verjee                                |
|                               | Simon      | Wan                                   |
| Freeman Hospital, Newcastle   | Ashraf     | Azzabi (PI)                           |
|                               | Craig      | Alderson                              |
|                               | Chris      | Barron                                |
|                               | Michelle   | Borthwick                             |
|                               | Julie      | Burton                                |
|                               | Kay        | Carson                                |
|                               | Fiona      | Chapman                               |
|                               | Sarah      | Cook                                  |
|                               | Fareeda    | Coxon                                 |
|                               | Sue        | Farrell                               |
|                               | Elaine     | Greaves                               |
|                               | Ahmed      | Hashmi                                |
|                               | Amanda     | Henderson                             |
|                               | Kathryn    | Hewitt                                |
|                               | Ben        | Hood                                  |
|                               | Thomas     | Jarvis                                |
|                               | Irene      | Jobson                                |
|                               | Najibah    | Mahtab                                |
|                               | Lesley     | Naik                                  |
|                               | Stephanie  | Needham                               |
|                               | Gemma      | O’Neill                               |
|                               | Ian        | Pedley                                |
|                               | Sindhu     | Ramamurthy                            |
|                               | Zarine     | Razvi                                 |
|                               |            | (continued in next column)            |

(continued in next column)
## Participating Hospitals in Descending Order of the Number of Patients Registered With All Staff Listed (N = 2,076) (continued)

| Hospital                        | First Name | Surname (principal investigator [PI]) |
|---------------------------------|------------|--------------------------------------|
| Belfast City Hospital           | Victoria   | Coyle (PI)                           |
|                                 | Conal      | Askin                                |
|                                 | Ellen      | Brown                                |
|                                 | Karen      | Campfield                            |
|                                 | Catherine  | Davidson                             |
|                                 | Michael    | Hanna                                |
|                                 | Diane      | Law                                  |
|                                 | Alison     | McKeever                             |
|                                 | Aine       | McKeown                              |
|                                 | Damian     | McManus                              |
|                                 | Linda      | McNeice                              |
|                                 | Karen      | Parsons                              |
|                                 | Miranda    | Reid                                 |
|                                 | Fiona      | Tarpey                               |
|                                 | Joanne     | Todd                                 |
|                                 | Paul       | Ward                                 |
|                                 | Richard    | Wilson                               |
| Dorset County Hospital          | Amelie     | Harle (PI)                           |

(continued in next column)

| Hospital                        | First Name | Surname (principal investigator [PI]) |
|---------------------------------|------------|--------------------------------------|
| Great Western Hospital          | Sarah      | Lowndes (PI)                         |
|                                 | Graham     | Brown                                |
|                                 | Christopher| Clarke                               |
|                                 | Amanda     | Colston                              |
|                                 | Jan        | Dodge                                |
|                                 | Eva        | Fraile                               |
|                                 | Sarah      | Grayland                             |
|                                 | Lesley     | Haxton                               |
|                                 | Lawrence   | John                                 |
|                                 | Jean       | Kordula                              |
|                                 | Lynsey     | Kyeremeh                             |
|                                 | Donna      | Lake                                 |
|                                 | Catherine  | Lewis Clarke                         |
|                                 | Sarah      | Long                                 |
|                                 | Dorota     | Marciniak                            |
|                                 | Laura      | McCafferty                           |
|                                 | Darren     | McFadden                             |
|                                 | Sue        | Meakin                               |
|                                 | Chanelle   | Meyer                                |
|                                 | Tim        | Owen                                 |
|                                 | Cerila     | Parajaes                             |
|                                 | Ronak      | Patel                                |
|                                 | Suzannah   | Peggler                              |
|                                 | Caroline   | Pensotti                             |
|                                 | Joseph     | Stevens                              |
| Milton Keynes University Hospital| Wasiru    | Saka (PI)                            |
|                                 | Ann        | Abraham                              |
|                                 | Hannah     | Ansell                               |
|                                 | Sam        | Bosompern                            |
|                                 | Matthew    | Burnett                              |
|                                 | Chris      | Ford                                 |

(continued on following page)
| Hospital                     | First Name  | Surname (principal investigator [PI]) |
|------------------------------|-------------|---------------------------------------|
| New Cross Hospital           | Simon       | Grumett (PI)                          |
|                              | Syed        | Asghar                                |
| Pilgrim Hospital             | Zuzana      | Stokes (PI)                           |
|                              | Antoinette  | Adu                                   |
|                              | Simon       | Archer                                |
|                              | Gloria      | Barone                                |
|                              | Jayne       | Borley                                |
|                              | Wendy       | Deamer                                |
|                              | Jo          | Fletcher                              |
|                              | Matthew     | Flook                                 |
|                              | Amy         | Kirkby                                |
|                              |             | (continued in next column)            |

| Hospital                     | First Name  | Surname (principal investigator [PI]) |
|------------------------------|-------------|---------------------------------------|
| Victoria                     | Knight      |                                       |
| Tara                         | Lawrence    |                                       |
| Beverley                     | Mashegede   |                                       |
| Helen                        | Palmer      |                                       |
| Kerry                        | Pettitt     |                                       |
| Gunjan                       | Phalod      |                                       |
| Manuel                       | Ruiz-Echarri|                                       |
| Gemma                        | Sankey      |                                       |
| Thomas                       | Sheehan     |                                       |
| Rebecca                      | Spencer     |                                       |
| Kinga                        | Szymiczek   |                                       |
| Isobel                       | Thomas      |                                       |
| Rotherham District General Hospital | Joanne     | Hornbuckle (PI)                       |
| Matthew                      | Barnes      |                                       |
| Sarah                        | Besley      |                                       |
| Menedyth                     | Harris      |                                       |
| Kath                         | Lowe        |                                       |
| Scott                        | Nicol       |                                       |
| Susan                        | Oakley      |                                       |
| Amy                          | Rees        |                                       |
| Charlotte                    | Widdop      |                                       |
| Royal Bournemouth Hospital   | Tamas       | Hickish (PI)                          |
| Jocelyn                      | Ablorde     |                                       |
| Omolade                      | Bakarey     |                                       |
| Rachel                       | Bower       |                                       |
| Zoe                          | Clark       |                                       |
| Nicole                       | Davies      |                                       |
| Alison                       | Hogan       |                                       |
| Stephanie                    | Jones       |                                       |
| Tiffany                      | Joyce       |                                       |
| Maria                        | Lane        |                                       |
| Sharon                       | Megson      |                                       |
| Sandy                        | Presslee    |                                       |
| Linda                        | Purandare   |                                       |
| Tasliima                     | Rabbi       |                                       |
| Emma                         | Sharland    |                                       |
| Esther                       | Una Cidon   |                                       |
| Luke                         | Vamplew     |                                       |
| Jasmin                       | Webb        |                                       |

(continued on following page)
| Hospital | First Name | Surname (principal investigator [PI]) |
|----------|------------|--------------------------------------|
| Royal Marsden Hospital (London) | Ian | Chau (PI) |
| Helen | Breeze |
| Shirley | Clifton |
| Saoirse | Dolly |
| Sandra | Esteban Moreno |
| Lucy | Featherstone |
| Shelby | Hatt |
| Blanka | Hezelova |
| Alexander | Lee |
| Hazel | Lote |
| Lizzie | Love |
| Nnenna | Ngwu |
| Isma | Rana |
| Gihan | Ratnayake |
| Penny | Rogers |
| Clare | Saffery |
| Anna | Scott |
| Izelle | Ueckermann |
| Chloe | Westrip |
| Ian | Chau |
| Sally | Abdelmalik |
| Gayahri | Anandappa |
| Joo Ern | Ang |
| Thushasa | Ansari |
| Sheila | Azaji-Benjamin |
| Annette | Bryant |
| Shirley | Clifton |
| Richard | Crux |
| David | Cunningham |
| Sara | Diffley |
| Julie | Duncan |
| Laurence | Edwards |
| Sandra | Esteban Moreno |
| Lucy | Featherstone |
| Monika | Ferencova |
| Angela | Gillbanks |
| Sarneet | Kaur |
| Naila | Kaudeer |
| Shelize | Khakoo |
| Shannon | Kidd |
| Retchel | Lazaro Alcausi |

(continued in next column)