remained elusive. Here we present one possible cause: MAPK-driven KT stress. The hallmarks of KT stress include chronic KT- MT attachment instability in mitosis, dramatic changes in KT morphology, and increases in microtubule KT attachments and chromosome segregation errors, KT stress is lethal to cancer cells. However, stressed cells survive by relying on BUB1/Bub1 activity to strengthen KT- MT attachments. We first observed KT stress in GBM patient isolates, where ~60–70% display its hallmarks. We subsequently found that RAS or MEK activity is sufficient to induce KT stress in both CNS and non-CNS derived cell types. We propose that KT stress is caused by aberrant mitotic RAS/MAPK activity, which likely targets one or more KT proteins resulting in KT-MT attachment defects and chromosome mis-segregation. In addition, Dr. Jun Zhu’s lab has also created a computational classifier that can identify KT stressed cells and tumors based on the expression of 838 genes associated with KT stress, which can also be used to identify orthogonal therapeutic sensitivities. We will present these findings as well at this meeting.

CBIO-25. INTEGRATED MOLECULAR AND BH3 PROFILING OF THE INTRINSIC APOPTOTIC MACHINERY IDENTIFIES THERAPEUTIC VULNERABILITIES IN GLIOBLASTOMA

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Resistance to apoptosis is a hallmark of cancer. However, the underlying molecular mechanisms of intrinsic-apoptotic resistance in glioblastoma (GBM) remain largely unknown. Here we performed integrated molecular and functional characterization (via BH3 profiling) of the intrinsic apoptotic machinery in 50 GBM patient specimens. We found that, despite significant genetic heterogeneity of our GBM samples, all GBMs have a cross compensatory reliance on BCLXL and MCL1 for basal survival. Treatment with standard of care (e.g., temozolomide or radiation) caused minimal apoptotic stress, yet ablated the MCL-1 block in a p53-dependent manner, thus creating an exclusive dependence on BCLXL for survival in p53 wild-type GBM tumors. Consequently, BCLXL inhibition led to p53-dependent cell death with IR/TMZ in GBM tumors with intact p53 signaling. Importantly, the degree of synergistic cell kill was best predicted by combining molecular features with BH3 profiling, providing an integrated predictive signature in response to this novel therapeutic approach. Collectively, these studies identify mechanisms of intrinsic apoptotic resistance in both basal and treatment states of GBM and demonstrate how functional and molecular data can be complementary to robustly predict therapy-induced cell death.

COVID-19 AND NEURO-ONCOLOGY

COVID-01. ADAPTATION OF A GAMMA KNIFE ICON STEREOTACTIC RADIOSURGERY PROGRAM IN THE FACE OF A GLOBAL COVID-19 PANDEMIC

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PURPOSE: The COVID-19 pandemic necessitated drastic and rapid changes throughout the field of radiation oncology. Available guidelines called for reduced frame use, postponing non-urgent cases, and reducing the number of fractions delivered. Our institution enacted many of these guidelines, and herein we show the resultant effect on patient treatments on our Gamma Knife Icon system. METHODS & MATERIALS: In early to mid-March of 2020 our institution rapidly implemented suggested changes according to ASTRO and other consensus guidelines as they relate specifically to stereotactic radiosurgery in the COVID-19 era. We reviewed the GK Icon schedule at our institution between January 01 and April 30, 2020. We documented the treatment age, condition treated, technique (frame vs. mask), and number of frac- tions. We then tabulated and graphed the number of patients, framed cases, and fractions across that time period. RESULTS: Seventy-seven patients were treated on the GK Icon between January and April 2020, a total of 231 fractions. The number of unique patients per month varied from 18 (April) to 22 (January). Of the 77 patients only 5 were treated using a frame. The number of fractions per month decreased significantly over time, from 70 in January to 34 in April. Likewise, the percentage of single fraction cases increased from 4.5% per month in January to 67% in April. CONCLUSIONS: The results presented here show that it is possible to quickly and efficiently change work flows to allow for reduced frame utilization and frame use in the time of a global pandemic. Multidisciplinary cooperation and ongoing communication are integral to the success of such programs.

COVID-02. ADAPTING RNA-NANOPARTICLE VACCINES FROM GlioBLASTOMA TO SARS-COV-2

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BACKGROUND: Glioblastoma (GBM) can be an effective teacher in the war on COVID-19, as an operative vaccine for either must elicit near-immediate protective responses that overcomes disease heterogeneity and immune suppression. Current prophylactic strategies for GBM do not utilize mRNA vaccines targeting small fragments of the SARS-CoV-2 genome, but these may not induce robust T cell responses or elicit immunity quickly enough. OBJECTIVE: We sought to adapt an FDA-IND approved mRNA vaccine in GBM against COVID-19 for: 1) activation of near immediate immune responses targeting full-length glioblastoma antigens or SARS-CoV-2 structural proteins. RESULTS: In small and large animal models, RNA-NPs safely mimic viremia activating the quiescent immune system in only a few hours for induction of protective immunity against its mRNA payload. RNA-NP activation results in overexpression of SARS-CoV-2 spike peptide mix. We also found increased release of MIP-1-alpha (i.e. CCL3) previously shown by our group (Mitchell et al. Nature 2015) to be responsible for Th1 mediated memory recall to infectious vaccine antigens in GBM pa- tients. CONCLUSION: SARS-CoV-2 RNA-NPs elicit memory recall response after vaccination. We have obtained FDA-IND approval (BB-19304, Sayour in GBM with SARS-CoV-2 specific amendment (BB-20871) to support first-in-human trials of RNA-NPs targeting both GBM and COVID-19.

COVID-03. ASSESSING THE IMPACT OF CORONA VIRUS 19 PANDEMIC ON NEURO-ONCOLOGY AT GUY’S CANCER CENTRE LONDON

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BACKGROUND: Immunosuppressive treatment increases COVID-19 risk. Neuro-oncology patients may not qualify for ILU if they deteriorate, but without oncological treatment, prognosis is poor. The pandemic has seen the introduction of new guidelines; including alternative treatment schedules which balance risks of contracting COVID-19, against safely delivering cancer treatment. We assess COVID-19 impact on neuro-oncology treatment at Guy’s Cancer Centre, London. METHODS: Notes of patients seen March-April 2020 were reviewed. Demographic data, tumour grade, treatment and changes due to COVID-19 recorded. RESULTS: 111 patients were identified (69 male: 42 female, median age 51years). 65 were WHO Grade 4, 24 Grade 3, 17 Grade 2. 84% (96) had a radiological diagnosis; 4 had hypofractionated radiotherapy (30Gy in #) to minimise hospital visits; 6 had no chemotherapy (5 were unembrylated /age, 2 patient choice); - 4 switched from PCV to Lomustine; - 11 stopped chemotherapy early; - 50% (36) were given prophylactic GCs-F; - No patients were recruited for trials. 19 reported possible COVID-19 symptoms – 7 had delays and 3 stopped treatment. 4 tested COVID-19 positive (although not all tested), 1 died of COVID-19 (off treatment). Review of March-April 2020 service showed similar new patient referrals compared to the same time in 2019 (16 and 19 respectively). CONCLUSION: Despite concern about decreasing service, all 22 patients on board at 31st March and 1st April had a radiological diagnosis. 14% (32) of consultations were new patients treated on board. 15 had active-surveillance and 2 best-supportive care. To conclude, the pandemic has seen the introduction of new guidelines; including alternative treatment schedules which balance risks of contracting COVID-19, against safely delivering cancer treatment. We assess COVID-19 impact on neuro-oncology treatment at Guy’s Cancer Centre, London. METHODS: Notes of patients seen March-April 2020 were reviewed. Demographic data, tumour grade, treatment and changes due to COVID-19 recorded. RESULTS: 111 patients were identified (69 male: 42 female, median age 51years). 65 were WHO Grade 4, 24 Grade 3, 17 Grade 2. 84% (96) had a radiological diagnosis; 4 had hypofractionated radiotherapy (30Gy in #) to minimise hospital visits; 6 had no chemotherapy (5 were unembrylated /age, 2 patient choice); - 4 switched from PCV to Lomustine; - 11 stopped chemotherapy early; - 50% (36) were given prophylactic GCs-F; - No patients were recruited for trials. 19 reported possible COVID-19 symptoms – 7 had delays and 3 stopped treatment. 4 tested COVID-19 positive (although not all tested), 1 died of COVID-19 (off treatment). Review of March-April 2020 service showed similar new patient referrals compared to the same time in 2019 (16 and 19 respectively). CONCLUSION: Despite concern about decreasing new referrals during the pandemic, this wasn’t the case for our service. 77.5% of patients had no treatment changes due to COVID-19 and all 22 patients on trial were able to continue treatment throughout this period.

COVID-04. REAL-WORLD PERSPECTIVES: TUMOR TREATING FIELDS (TTTFIELDS) UTILITY TO OPTIMIZE TREATMENT OF PATIENTS WITH GlioBLASTOMA (GBM) AMIDST COVID-19 PANDEMIC

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INTRODUCTION: Due to the unprecedented, COVID-19 pandemic and resulting health/safety guidelines, rapid-adjustments to treatment plans
Abstracts

for patients battling glioblastoma (GBM; debilitating, aggressive cancer) were critical. Tumor Treating Fields (TTFields; FDA-approved for GBM; antimitotic device) are alternating electric fields (200 kHz) delivered through scalp-placed transducer arrays to target rapidly dividing GBM cells. Visitor restrictions at cancer-centers and often overburdened healthcare teams provided obstacles to cancer therapy. Health and safety of patients/caregivers, healthcare providers (HCPs), and patient Device Support Specialists (DSS) were critically important. To evaluate the impact of COVID-19 (device manufacturer) implemented strategies on overcoming limitations/restrictions to treatment-access during COVID-19. TREATMENT/PROTOCOL: TTFields (Optune) offers a viable noninvasive, built-in-care system for convenient at-home use. TTFields provides survival benefit with continuous, portable usage and is tolerable (no-related systemic effects) without overall impact on quality-of-life (except itchy skin). Novocure adopted/amended protocols to meet health guidance/regulation (ie, World Health Organization, Centers for Disease Control and Prevention, local, hospital/clinic directives). PER-SPECTIVES: COVID-19 forced a change in treatment patterns imposed by new safety signals were observed utilizing new approaches. CONCLU-SIONS: TTFields care-delivery has been transformed during COVID-19 and preemptively in regards to other future access-limiting events, with adoption of virtual-platforms/protocols, resulting in enhanced access and education for patients/caregivers and healthcare teams.

COVID-06. BRAIN TUMOURS AND COVID-19: THE PATIENT AND CAREGIVER EXPERIENCE

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BACKGROUND: Since the COVID-19 pandemic, thousands of medical procedures and appointments have been cancelled or delayed. The long-term effects of these drastic measures directly on brain tumour patients and their caregivers are unknown. The purpose of this study is to better understand how COVID-19 has affected this vulnerable population on a global scale.

METHODS: An online 79-question survey was developed by the IBTA in conjunction with the SNO COVID-19 Task Force. The survey was sent to over 120 brain tumour charities and for-not-profits worldwide and disseminated to brain tumour patients and caregivers. All responses were blinded. Both patient vs caregiver survey was by geographical region. RESULTS: In total, 1989 participants completed the survey from 33 countries, including 1459 patients and 530 caregivers. There were no significant differences in COVID-19 testing rates (p = 0.6622) or the number of positive cases for brain tumour patients between regions (p = 0.1068). Caregivers were significantly more anxious than patients (p = <0.0001). Patients from the Americas were most likely to have lost their jobs due to the pandemic, practiced self-isolation, and received telehealth services (p = <0.0001). Patients from Europe experienced the most treatment delays (p = 0.0031). Healthcare providers were ranked as the most trusted source of information. CONCLUSIONS: As a result of COVID-19, brain tumour patients and caregivers have experienced significant stress and anxiety. Healthcare providers are less visible, however, by the ongoing COVID-19 pandemic (and other historical circumstances of severe resource limitation in the healthcare system). We interrogate ethical considerations involved in the state of medical care as COVID-19 pandemic widened the gap for patients with cancer, in which the pillar of justice is exposed as internally divided. Specifically, we identify both patient-oriented and system-oriented principles of justice constituting a broader collective, unique among the classical four principles. This leads us to suggest a formal recognition of justice as a divided category, and a reclassification of the term into two subcategories which serve fundamentally different interests. The result is a more cohesive four principle approach in which all principles favour the deontological relationshions fostered between patients and providers, which exists in constant balance with the utilitarian interests of the broader medical system.

COVID-07. THE IMPACT OF COVID-19 ON PATIENTS AND CAREGIVERS AFFECTED BY BRAIN TUMOURS: THE PATIENT NAVIGATOR PERSPECTIVE

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BACKGROUND: Preliminary evidence indicates that glioma patients are at higher risk for COVID-19 complications due to systemic immunosup- pressive interventions in cancer care may lead to increased anxiety, but surveying patients/caregivers about their COVID-19 experi- ences is often limited by attainable sample sizes and over-reliance upon single-institution experiences. METHODS: To explore how COVID-19 is impacting brain tumor patients/caregivers across the U.S., we performed semi-structured interviews with brain tumor patient navigators employed by two different 501(c)3 nonprofit organizations. A semi-structured interview guide was used, utilizing prompts and open-ended questions to facilitate dialogue. A core set of COVID-19 topics were covered, including: financial impact of disease, psychosocial impact, disruptions in care access, clinical trials, psychosocial issues, end-of-life care. Interviews were audio-recorded, transcribed, and organized by discussion topic to identify emerging themes. For coding, two coders independently coded the transcripts within and between transcripts. RESULTS/CONCLUSIONS: Ten patient navigators were interviewed between April 15th and May 8th, with interviews lasting approximately one hour (range 38-77 minutes). Navigators reported having contact with 183 unique brain tumor families during the pandemic (range 7-38 families per navigator). High concordance emerged across narratives, revealing important considerations for the neuro-oncology work-force. The most prominent theme was increased caregiver burden, attributed to maintaining social distancing by reducing visits from home-health aides and friends/family. A related theme that applied to both patients and care-givers was increased social isolation due to social distancing, suspension of in-person support groups, and church/temple closures. Accessing clinical trials was a recurrent issue, exacerbated by patients’ increasing unwilling- ness to travel. Glioblastoma patients, especially those with recurrent tumors, expressed greater reluctance to travel. Access to standard-of-care treatment was rarely interrupted, but reduced access to supportive services – especially physical and occupational therapy – was identified as an emerging COVID-related deficiency in clinical care.

COVID-08. THE DIVIDED PRINCIPLE OF JUSTICE: ETHICAL DECISION-MAKING IN CANCER CARE DURING THE COVID-19 PANDEMIC

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The four-principle approach to medical ethics, balancing prima facie ob- ligations to beneficence, nonmalefore, autonomy, and justice, has sup- plied a common language for the application of ethical analysis to medical practice for the last four decades. The frayed edges of this edifice are visible, however, by the ongoing COVID-19 pandemic (and other his- torical circumstances of severe resource limitation in the healthcare system). We interrogate ethical considerations involved in the state of medical care as COVID-19 pandemic widened the gap for patients with cancer, in which the pillar of justice is exposed as internally divided. Specifically, we identify both patient-oriented and system-oriented principles of justice constituting a broader collective, unique among the classical four principles. This leads us to suggest a formal recognition of justice as a divided category, and a reclassification of the term into two subcategories which serve fundamentally different interests. The result is a more cohesive four principle approach in which all principles favour the deontological relationshions fostered between patients and providers, which exists in constant balance with the utilitarian interests of the broader medical system.

COVID-09. INVESTIGATION AND SUMMARY OF DIAGNOSIS AND TREATMENT OF NEUROLOGICAL TUMORS DURING COVID-19 IN CHINA

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In order to realize the condition of diagnosis and treatment of neuro- logical tumors in China during COVID-19, CNSO (China Anti-Cancer Association Neuro-Oncology Professional Committee) organized this ques- tionnaire survey. The survey was conducted online from June 3rd to 16th in 2020. A total of 373 replies were received and 370 were confirmed valid questionnaires. The respondents were mainly neurosurgeons, as well as radiotherapists and pathologists in general hospitals and specialized hos- pitals in 29 provinces and municipalities in China. The survey results are summarized as follows. Firstly, the number of outpatient and inpatient of neurological tumors significantly declined during the COVID-19 pandemic with the same period last year in more than 90% of hospitals surveyed, and a few specialized hospitals even stopped treatment due to the outbreak of COVID-19. Compelled by illness was the main reason for most of the patients to go to hospital. As the epidemic prevention and controlling, the normal treatment process for each patient was tedious than that for the same period before, and the costing time also turned longer. Most patients might feel poor medical experience, but they also expressed understanding for the delay caused by the epidemic prevention and controlling. Beyond the epidemic period, the participation in academic conferences or MDT decreased significantly for most doctors, and scientific research work even stopped in some hospitals. Online tools have risen as the primary means of communication, not only for academic communication but also for diagnosis and treatment works. More than 90% of doctors believe the