Retrospective Study

Trends in the management of anorectal melanoma: A multi-institutional retrospective study and review of the world literature

Josh Bleicher, Jessica N Cohan, Lyen C Huang, William Peche, T Bartley Pickron, Courtney L Scaife, Tawnya L Bowles, John R Hyngstrom, Elliot A Asare

ORCID number: Bleicher J 0000-0001-6137-4426; Jessica N Cohan 0000-0002-5461-4716; Lyen C Huang 0000-0002-8605-2631; William Peche 0000-0001-9770-2137; T Bartley Pickron 0000-0002-0880-1959; Courtney L Scaife 0000-0003-2497-4961; Tawnya L Bowles 0000-0002-1883-1510; John R Hyngstrom 0000-0002-4833-3838; Elliot A Asare 0000-0002-0176-3865.

Author contributions: Bleicher J, Bowles TL, Hyngstrom JR and Asare EA designed the study and created the methodology; Bleicher J and Asare EA performed data analysis; Bleicher J created the first draft of the manuscript; Asare EA supervised the research; all authors participated in data acquisition and provided edits and helped with subsequent writing.

Institutional review board statement: The Institutional Review Boards of the University of Utah and Intermountain Health Care approved this study.

Conflict-of-interest statement: I confirm that I have no financial disclosures to declare. As the corresponding author for this manuscript, I also declare that none of my co-authors have financial disclosures to declare.

Abstract

BACKGROUND
Anorectal melanoma (ARM) is a rare disease with a poor prognosis. Evidence on optimal treatment is limited and surgical management varies widely. We hypothesized that the frequency of abdominoperineal resection used as primary treatment of ARM has decreased over the past several decades.

AIM
To update our understanding of outcomes for patients with ARM and analyze management trends around the world.

METHODS
This is a multi-institutional, retrospective study of patients treated for ARM at 7 hospitals. Hospitals included both large, academic, tertiary care centers and smaller, general community hospitals. Using prospectively maintained institutional tumor registries, we identified 24 patients diagnosed with ARM between January 2000 and May 2019. We analyzed factors prognostic for recurrence and survival. We then used Cox regression to measure overall survival (OS) and melanoma-specific survival. We also performed a literature review to assess trends in surgical management and outcomes.

RESULTS
Of the 24 patients diagnosed with ARM, 12 (50.0%) had local, 8 (33.3%) regional,
Anorectal melanoma (ARM) is a rare malignancy with a poor prognosis. The estimated annual incidence in the United States is less than 5 cases per 10 million[1]. Overall 5-year survival is between 10% and 20%[2,3]. This low survival is due to the late diagnosis of most tumors and aggressive biology of ARM[4]. Most tumors are first recognized from symptoms such as bleeding, obstruction, pain, or changes in bowel habits[4,5]. When these tumors are recognized, they are often misdiagnosed as hemorrhoids or other benign anorectal pathology[1].

National Clinical Cancer Network (NCCN) guidelines on melanoma do not currently include recommendations for treatment of ARM[6]. Without guidelines, and due to the rare nature of the tumor, treatment is highly variable. Controversy exists over optimal primary surgical therapy. Some advocate abdominoperineal resection (APR) for initial treatment, while others report similar oncologic outcomes with wide excision (WE) alone[7-9]. As outcomes are universally poor, many providers recommend the less invasive and lower morbidity WE as primary treatment[8,9]. Optimal primary nodal management strategy is also unknown. Non-surgical therapy is even more varied. Radiotherapy, chemotherapy, and targeted therapies (including interferon, checkpoint-inhibitors, anti-BRAF therapy, and tyrosine kinase inhibitors) have all been used alone or in various combinations[10-17]. No clear treatment strategy has emerged as the gold standard for treatment of this rare but aggressive disease.

Core Tip: This is a retrospective study to evaluate current trends in management of anorectal melanoma (ARM). On review of 24 patients from 7 hospitals in Utah, we found that ARM is a highly lethal disease with overall survival of 18.8 mo (interquartile range 13.5-33.9) and no 5-year survivors. Only 2 patients underwent abdominoperineal resection (APR) as primary surgical management. Review of the literature demonstrated wide variation in surgical management of ARM over time and around the world. Whether APR or wide excision was used, outcomes remained poor. With this data, we recommend that surgical management should aim to minimize morbidity.

CONCLUSION
There is wide variation in the management of ARM and survival outcomes remain poor regardless of approach. Surgical management should aim to minimize morbidity.

Key Words: Melanoma; Anorectal melanoma; Literature review; Melanoma surgery; Surgical oncology; Colorectal surgery

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.
Given the lack of guidelines and variability in reported practice patterns, we analyzed outcomes from a multi-institutional cohort of patients with ARM. We also provide an updated review of the literature to compare outcomes from across the decades and around the world. This review allows for analysis of overall trends to help guide treatment decisions for patients with ARM.

**MATERIALS AND METHODS**

**Study design**

We retrospectively reviewed patients diagnosed with ARM between January 1, 2000 and January 1, 2019. This allowed for at least 12 mo of follow-up for all patients. Patients were identified using international classification of diseases-9/10 codes in prospectively maintained institutional tumor registries at 7 centers near Salt Lake City, Utah. These centers included the University of Utah Huntsman Cancer Institute and 6 hospitals affiliated with Intermountain Health Care. All names were linked across institutions to ensure only unique patients were included in the study.

**Data Collection**

We abstracted data from the electronic medical record and institutional tumor registries. Manual chart review was performed for all records to verify data and obtain additional information. Data abstracted includes patient demographics, primary tumor characteristics, treatment details, and cancer-related outcomes. Both adjuvant therapy and therapy at time of relapse were recorded. Specific chemotherapy and immunotherapy agents were noted. Vital status was available for all but one patient.

Extent of disease was categorized into local, regional, or distant depending on whether disease was confined to the anorectum, involved regional lymph nodes, or other organs\[3\]. Extent of disease classification was based on clinical documentation. The extent of primary surgical therapy was also determined by clinical documentation. The Institutional Review Boards of the University of Utah and Intermountain Health Care approved this study.

**Statistical analyses**

Statistical analyses were performed using Stata Version 15.1 (Stata Corp, College Station, TX, United States). We analyzed patient demographics, initial tumor characteristics, and treatment details using descriptive statistics. We calculated median time to recurrence, melanoma-specific survival (MSS), and overall survival (OS) for the cohort and determined MSS and OS at 2, 3, and 5-year intervals. Patients with unknown survival outcomes were excluded from OS analysis and patients with unknown cause of death were excluded from MSS analysis. We graphically evaluated these outcomes using the Kaplan-Meier method. Time-zero for all time-to-event outcomes was the date of diagnosis. Recurrence was defined as re-appearance of disease on physical exam or radiographically in patients who had been initially rendered free of disease after initial treatment. Patients were determined to be free of disease following initial therapy based on intention to treat, as described in clinical documentation.

Cox regression was used to assess for any factors associated with survival. Results were considered statistically significant if the two-sided $P < 0.05$. Analysis of outcomes associated with different surgical and non-surgical treatment options was performed in a similar fashion. Multivariable analysis was not performed because of the small sample size of this cohort.

**Review of the literature**

We performed a literature review using the PubMed database. The 2009 PRISMA checklist was used to ensure transparent reporting of search and review methodology\[18\]. The search term used was “ARM.” Search results did not differ significantly when “anal melanoma” or “rectal melanoma” were considered separately. All English language articles were included. Articles were excluded if they did not describe outcomes of a unique cohort of at least 10 patients. When multiple articles described overlapping patient cohorts, the most recent and inclusive article was used. Studies describing patient outcomes from national databases in the United States were excluded, as these patients are often represented in other institutional studies. National database studies from other countries were included when other cohorts from these countries did not exist. All titles and abstracts were reviewed for
inclusion.

Once this review was complete, all full-length articles were reviewed. Outcomes of interest were surgical management of patients, median OS, and 5-year OS. No summary of outcomes was performed because of the significant heterogeneity among the various studies.

**RESULTS**

Twenty-four patients met inclusion criteria. Two-thirds of patients were female, with median age of 65.5 [interquartile range (IQR) 54-76] (Table 1). Patients were from five different states (UT, ID, WY, NV, CO) and approximately 20% of patients were from rural communities. Of 13 patients with information on Breslow depth, 7 (53.8%) were > 5 mm. There were 9 (37.5%) patients whose melanoma exhibited ulceration (Table 1). Half of the patients had advanced disease at diagnosis; 8 with nodal disease and 4 with distant metastases.

Fifteen patients (62.5%) underwent WE at diagnosis and 2 patients (8.3%) underwent APR (Table 2). Seven patients (29.2%) received biopsy alone, including 2/4 patients with distant disease at diagnosis. The primary operation took place at a median of 27 d after diagnosis (IQR 0-47). Sentinel lymph node biopsy (SLNB) was performed in 6 (25%) patients. Of those with local or nodal disease, nearly half of patients received surgery alone as primary management. The remainder of patients received systemic therapy of some form following surgical resection. There was wide variation in adjuvant treatment. Some patients received chemotherapy, radiation, interferon, or checkpoint-inhibitor therapy alone; others received these in various combinations (Table 2).

Of 21 patients with complete follow-up data, only 2 (9.5%) remained free of disease after resection. One of these patients died of metastatic colon adenocarcinoma 13.9 mo after ARM diagnosis. The other patient was alive at last follow-up with no evidence of disease 21.4 mo from diagnosis. Excluding the 4 patients with distant disease at diagnosis, 3 (20.0%) of the remaining 15 patients were never free of disease and the remaining 12 (80.0%) recurred after initial treatment. One patient who was never free of disease underwent APR as salvage therapy. Median time to recurrence was 10.4 mo (IQR 7.5-17.2). At the time of recurrence, 4 patients (33.3%) opted not to pursue further therapy given their age, comorbidities, and/or overall prognosis. Of those who received further treatment (n = 8), only 1 patient had surgery (repeat WE and bilateral inguinal lymph node dissection). Use of systemic therapy was highly variable. Individual patient treatments and outcomes are shown in Supplementary Table 1.

Survival status was known for all but 1 patient. Of these 23 patients, 1 (4.3%) was alive at last follow-up (21.4 mo from diagnosis). Fourteen (60.9%) died from ARM. The cause of death was unknown for 7 (30.4%) patients. Median OS was 18.8 mo (IQR 13.5-33.9) with 0 survivors at 5 years (Figure 1A). Two-year OS was 21.0% (95%CI: 6.8%-40.3%) and 3-year OS was 10.4% (95%CI: 1.8%-27.9%). Median MSS was 19.5 mo (IQR 14.8-35.1) (Figure 1B). Two-year MSS was 29.1% (95%CI: 9.1%-53.0%) and 3-year MSS was 14.6% (95%CI: 2.4%-37.0%). Excluding patients with distant disease at diagnosis, median OS was 19.9 mo (IQR 16.0-35.1) with 2-year OS of 25.5% (95%CI: 8.2%-47.3%) and 3-year OS of 12.7% (95%CI: 2.2%-33.0%). Median MSS was 19.9 mo (IQR 16.4-39.8) with 2-year MSS of 36.4% (95%CI: 11.2%-62.7%) and 3-year MSS of 18.2% (95%CI: 2.9%-44.2%).

Age, sex, rural location, mitoses, ulceration, and Breslow depth were not prognostic of OS. Patients with distant disease at diagnosis had higher risk of mortality than patients with local disease [hazard ratio (HR) = 14.6 (95%CI: 2.5-86.7)] or nodal disease [HR = 14.4 (95%CI: 2.2-92.1)]. No differences in OS were noted for patients who underwent APR vs WE as their primary operation [HR = 1.4 (95%CI: 0.3-6.8)]. There was no significant difference in OS between patients who underwent nodal surgery [SLNB or completion lymph node dissection (CLND)] and those who did not [HR = 0.4 (95%CI: 0.1-1.1)]. Exclusion of patients with distant disease at diagnosis did not alter these results. No individual adjuvant therapy (immunotherapy, radiation, or chemotherapy) demonstrated a benefit over another therapy for patients with local or nodal disease treated with surgery as initial treatment.

**Review of the literature**

This search revealed 360 unique articles, of which 33 were included for review (Figure 2). Cohorts differed across studies, with some including all patients diagnosed with ARM and others limited to only patients with local or nodal disease or patients...
Table 1 Demographics and primary tumor characteristics for cohort with anorectal melanoma (n = 24)

| Classification                          | n    |
|-----------------------------------------|------|
| Age, years (median, IQR)                | 65.5 (54.76) |
| ≤ 50                                    | 3 (12.5) |
| 51–60                                   | 7 (29.2) |
| 61–70                                   | 6 (25.0) |
| 71–80                                   | 6 (25.0) |
| > 80                                    | 2 (8.3) |
| Sex                                     |       |
| M                                       | 8 (33.3) |
| F                                       | 16 (66.7) |
| Race                                    |       |
| White                                   | 23 (95.8) |
| Latino                                  | 1 (4.2) |
| Rural                                   |       |
| Yes                                     | 5 (20.8) |
| No                                      | 19 (79.2) |
| Breslow depth (mm)                      |       |
| ≤ 5                                     | 6 (25.0) |
| > 5                                     | 7 (29.2) |
| Unknown                                 | 11 (45.8) |
| Ulceration                              |       |
| Present                                 | 9 (37.5) |
| Absent                                  | 2 (8.3) |
| Unknown                                 | 13 (54.2) |
| Mitoses                                 |       |
| > 1                                     | 7 (29.2) |
| Unknown                                 | 17 (70.8) |
| Stage                                   |       |
| I                                       | 12 (50.0) |
| II                                      | 8 (33.3) |
| III                                     | 4 (16.7) |

IQR: Interquartile range.

treated with curative intent. Twenty-five studies reported median OS (Table 3). Median OS ranged from 7-49.5 mo and 21 (84%) studies had median OS < 25 mo. There was wide variation in the type of surgical management across studies. At some centers, all patients received WE while other centers treated all patients with APR. Eight studies achieved a 5-year OS rate of 20%. Three of these studies included patients diagnosed before 1980, with 1 study including patients from the 1930s. The other five study cohorts spanned into the 2000s. Surgical management of patients was mixed in this subset of studies. In a study of 54 patients with ARM treated at MD Anderson Cancer Center (MDACC) from 1989-2008, all patients with local disease underwent WE followed by radiation therapy and a 5-year OS of 30% was reported.

In another study from South Korea, authors described 12 patients who underwent APR and 7 who underwent WE with significantly improved OS with APR compared to WE. In the remainder of studies, 3 studies reported no significant differences between APR and WE and 3 did not report results of this comparison. No other dominant themes in surgical or non-surgical treatment were noted across these studies with superior survival outcomes.

Across all studies, the number of APRs was similar to WEs. In total, 427 patients had APR and 436 underwent WE. Studies from the same institution at different time points showed a trend towards performing fewer APRs with time. In two studies from Memorial Sloan Kettering Cancer Center (MSKCC) looking at cohorts from 1950-1977 and 1984-2003, 73.3% of patients underwent APR in the older cohort compared to 41.3% in the more recent cohort. At MDACC, Ross et al. reported APR in 53.8% of patients from 1952-1988 while Kelly et al. reported exclusive treatment with WE.
Table 2 Treatment details for cohort with anorectal melanoma (n = 24)

| Treatment                                      | n   | Percentage |
|------------------------------------------------|-----|------------|
| Primary operation, n                          |     |            |
| WE                                            | 15  | 62.5       |
| APR                                           | 2   | 8.3        |
| Biopsy alone                                  | 7   | 29.2       |
| Primary nodal operation, n                    |     |            |
| SLNB                                           | 6   | 25.0       |
| CLND                                           | 3   | 12.5       |
| None                                           | 15  | 62.5       |
| Adjuvant therapy, n¹                            |     |            |
| Chemotherapy alone                             | 0   | 0          |
| Radiation alone                                | 1   | 4.2        |
| Interferon alone                               | 3   | 12.5       |
| Checkpoint Inhibitor                           | 3   | 12.5       |
| Combination chemotherapy/radiation             | 2   | 8.3        |
| Combination chemotherapy/immunotherapy         | 3   | 12.5       |
| Combination radiation/immunotherapy           | 1   | 4.2        |
| None                                           | 11  | 45.8       |
| Surgery at recurrence²                         |     |            |
| APR                                           | 1   | 9.1        |
| WE                                            | 1   | 9.1        |
| Non-operative therapies at recurrence²        |     |            |
| Chemotherapy                                  | 1   | 9.1        |
| Radiation                                     | 0   | 0          |
| Interferon                                    | 0   | 0          |
| Checkpoint Inhibitor                           | 2   | 18.2       |
| Combination chemotherapy/radiation             | 4   | 26.7       |
| Combination chemotherapy/immunotherapy         | 2   | 13.3       |
| Combination radiation/immunotherapy           | 2   | 13.3       |

¹Excluding patients with distant disease at diagnosis (n = 4).
²Percentages calculated from total patients with recurrence who underwent treatment (n = 8).
APR: Abdominoperineal resection; WE: Wide excision; SLNB: Sentinel lymph node biopsy; CLND: Completion lymph node dissection.

between 1989-2008, as noted previously[10,27].

Geographic variation in surgical management exists. In United States cohorts, 45.7% (132/289) of surgical patients underwent APR, down to 24.3% over the past 40 years (35/144). European cohorts were similar with 45.1% of patients undergoing APR (123/273). Asian (China, South Korea, Japan, and Taiwan) and Indian cohorts had higher rates of APR with 69.9% (200/286) and 79.7% (51/64) of patients receiving APR as primary surgical therapy respectively. Das et al[19] and Ranjith et al[20] report cohorts from India with 100% of patients undergoing APR[19,20].

DISCUSSION

Dr. George Pack wrote in 1967, “cures are possible although they do not occur with encouraging frequency[19].” This study confirms the dismal prognosis associated with ARM. Only 1 patient from our study cohort was alive at last follow up, and there were no 5-year survivors. Only 6/33 studies reviewed reported a 5-year OS > 20%, and some of these studies included only patients with local disease. Most studies reported median OS of less than 2 years, and many less than 1 year. There is no compelling evidence from this review that a significant improvement in survival has been made for patients with ARM since 1967.

This study also demonstrates the wide variation in surgical treatment for ARM, both
| Ref.                  | Date published | Location                                         | Dates included | Sample size | Median age | M/F (n) | APR/WE (n) | Median OS | APR vs WE (% survival to 5 yr) | Overall 5 yr survival (%) |
|----------------------|----------------|--------------------------------------------------|----------------|-------------|------------|---------|-----------|-----------|-------------------------------|---------------------------|
| Pack et al[40]       | 1967           | Pack Medical Foundation, United States           | 1930-1965      | 20          | 53.5₁      | 5/15    | -         | -         | -                             | 5                         |
| Abbas et al[41]      | 1980           | Roswell Park Memorial Institute, United States   | 1930-1979      | 20          | 61.7       | 4/16    | 11/7      | 18.8¹     | 20.1 mo vs 8.5 mo³             | 7                         |
| Ward et al[42]       | 1986           | St. Mark's Hospital, United Kingdom              | 1932-1982      | 21          | -          | 12/9    | 9/6       | 8.8²      | -                             | 0                         |
| Thibault et al[23]   | 1996           | Mayo Clinic, United States                      | 1939-1993      | 50          | 63¹        | 15/35   | 26/10     | 26₁²      | 18 vs 19                       | 22                        |
| Wanebo et al[43]     | 1990           | Memorial Sloan Kettering Cancer Center, United States | 1950-1977     | 36          | 60         | 15/21   | 22/8      | 14        | 16/7 mo vs 21.5 mo³¹        | 8                         |
| Ross et al[47]       | 1990           | MD Anderson Cancer Center, United States         | 1952-1988      | 32          | -          | -       | 14/12     | 18.6      | 19.5 mo vs 18.9 mo³             | 3                         |
| Dodds et al[16]      | 2019           | Melanoma Institute Australia, Australia          | 1958-2016      | 43          | 61         | 21/22   | 20/15     | 24        | -                             | 16                        |
| Siegal et al[14]     | 1983           | Sheba Medical Center, Israel                     | 1960-1981      | 30          | 64¹        | 13/17   | 15/9      | 10.5¹     | -                             | 7                         |
| Roumen et al[48]     | 1996           | Eindhoven Cancer Registry, Netherlands           | 1960-1995      | 63          | 66         | 27/36   | 21/18     | -         | -                             | 6                         |
| Nilsson et al[45]    | 2010           | Swedish National Cancer Registry, Sweden         | 1960-1999      | 251         | 73         | 101/150 | 66/86     | 11.2      | 7 vs 15, P = 0.08             |                           |
| Podnos et al[46]     | 2006           | City of Hope National Medical Center, United States | 1973-2001     | 126         | 69.2¹     | 39/87   | -         | 15        | -                             | 19                        |
| Silingsuff et al[41] | 1990           | Duke University Medical Center, United States    | 1974-1988      | 24          | 64¹        | 7/17    | 13/8      | 18        | 18 vs 12                       | 8                         |
| Belli et al[49]      | 2008           | National Institute of Cancer, Italy              | 1975-2006      | 40          | 63         | 19/21   | 13/18     | 17        | 18.5 vs 18.5, P = 0.97        |                           |
| Che et al[22]        | 2011           | Peking Union Medical College, China              | 1975-2008      | 56          | -          | 22/34   | 36/20     | 21        | 24.6 vs 9.9, P = 0.65         | 20                        |
| Pessaux et al[50]    | 2004           | Institut Gustave Roussy, France                  | 1977-2002      | 30          | 58.1       | 7/23    | 9/21      | 17        | 16 vs 33                       | 17                        |
| Ramakrishnan et al[11] | 2008       | Cancer Institute (WIA), India                   | 1980-2004      | 63          | -          | 34/29   | 3/8       | 9.5³      | -                             | 5                         |
| Yeh et al[28]        | 2006           | Memorial Sloan Kettering Cancer Center, United States | 1984-2003     | 46          | 59         | 18/28   | 19/27     | 39⁵      | 32 vs 35, P = 0.66²           |                           |
| Homsi et al[40]      | 2007           | H. Lee Moffitt Cancer Center, United States      | 1987-2004      | 12          | 67         | 5/9     | 5/6       | -         | -                             |                           |
| Bullard et al[51]    | 2003           | University of Minnesota, United States           | 1988-2002      | 15          | 65¹        | 6/9     | 4/11      | 18⁸      | 14 mo vs 19 mo³                |                           |
| Kelly et al[40]      | 2010           | MD Anderson Cancer Center, United States         | 1989-2008      | 54          | 61         | 19/35   | 0/54      | 29        | -                             | 30                        |
| Das et al[40]        | 2003           | Tata Memorial Hospital, India                    | 1990-2001      | 72          | 49¹        | 20/52   | 24/0      | 13¹²     | -                             | 8²                        |
| Hicks et al[28]      | 2014           | John Hopkins Hospital, United States             | 1991-2012      | 18          | 64         | 10/8    | 7/11      | 15.5     | 11.5 mo vs 13.5 mo, P = 0.75  |                           |
| Yen et al[50]        | 2013           | Chang Gung Memorial Hospital, China              | 1993-2011      | 22          | 58.4¹      | 8/14    | 12/8      | -         | 0 vs 28.6, P = 0.06           | 9                         |
| Zhang et al[7]       | 2010           | First Affiliated Hospital of Guangxi Medical University, China | 1995-2007     | 54          | 54         | 21/33   | 39/15     | 25        | 30 vs 16, P = 0.28           | 26                        |
within and between medical centers. Geographic variation also exists, with United States and European centers more likely to perform WE and Asian and Indian centers more likely to perform APR. This finding was true in our cohort, with few patients undergoing APR. While low sample size limits analysis, there was no difference in survival outcomes between patients undergoing WE vs APR. Multiple other groups have demonstrated similar or better outcomes with WE compared to APR\(^{19,20}\). This same conclusion has been reached using larger cohorts from Surveillance, Epidemiology, and End Results and National Cancer Database (NCDB)\(^{31,32}\). A prior systematic review concluded that while APR may reduce local recurrence, there is no improvement in OS or recurrence-free survival compared to WE\(^{33}\).

WE allows for avoidance of a colostomy and significantly reduced morbidity compared to APR. A study of 49 patients undergoing WE demonstrated the safety of this procedure; 3 patients had minor infections requiring antibiotics and 1 patient required a second operation for postoperative bleeding. No other complications from surgery occurred\(^{6}\). While most studies of APR for ARM have not reported complication rates, APR for other indications is known to be associated with significant morbidities. Perineal wound complications occur in up to 40% of patients and 50% of patients develop genitourinary and/or sexual dysfunction postoperatively\(^{33}\). No studies currently exist in ARM that compare quality of life between WE and APR\(^{31}\). Some centers continue to routinely perform APR for ARM patients; however, we did not find evidence in this review to support this practice\(^{31,33}\).

Nodal management also differs widely. In our cohort, there were no significant differences in survival outcomes between patients who underwent initial nodal surgery (SLNB or CLND) and those who did not. Nearly 2/3 of patients did not receive any nodal staging or treatment. Older studies hypothesized that the benefit of APR was largely secondary to the mesorectal lymphadenectomy performed with this procedure\(^{6}\). However, Yeh et al\(^{28}\) found that the presence of lymph node metastases had no prognostic significance on survival in 19 patients who underwent APR at MSKCC\(^{28}\). Many patients in this cohort received local surgery alone and did not receive additional therapy until the time of recurrence. Some of these patients likely had unidentified nodal disease at the time of initial surgery. If patients had undergone SLNB and were found to have positive nodal disease, adjuvant systemic therapy could have been initiated sooner. The impact this may have had on survival is unknown. This review did not find studies with large enough patient numbers to make

| Bleicher J et al. Trends in anorectal melanoma management |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Sahu et al\(^{26}\) | 2017 | Tata Memorial Hospital, India | 2013-2015 | 37 | 54 | 25/12 | - |
| Nusrath et al\(^{27}\) | 2018 | Basavatarkakam Indo American Cancer Hospital, India | 2010-2015 | 30 | 50 | 15/15 | 13 |
| Ren et al\(^{28}\) | 2018 | Fudan University Shanghai Cancer Center, China | 2005-2017 | 60 | 61 | 18/42 | 38/22 |
| Ranjith et al\(^{29}\) | 2018 | Regional Cancer Center Thiruvananthapuram, India | 2001-2013 | 31 | 56 | 12/19 | 9/0 |
| Miguel et al\(^{30}\) | 2015 | IPOFG, Portugal | 2000-2011 | 10 | 70.5 | 2/8 | 5/1 |
| Choi et al\(^{31}\) | 2010 | Samsung Medical Center, South Korea | 1999-2008 | 19 | 61 | 8/11 | 12/7 |
| Belbaraka et al \(^{32}\) | 2012 | National Institute of Oncology, Morocco | 1998-2007 | 17 | 58\(^1\) | 12/5 | 7/3 |
| Ishizone et al\(^{33}\) | 2008 | Shinshu University Hospital, Japan | 1997-2006 | 79 | 65.8\(^1\) | 34/45 | 63/14 |
| Aytaç et al\(^{34}\) | 2010 | Uludag University, Turkey | 1997-2004 | 14 | 58 | 8/6 | 11/3 |

\(^1\)Mean reported instead of median.
\(^2\)Only cases treated with curative intent included in analysis.
\(^3\)Median overall survival (OS) [abdominoperineal resection (APR) vs wide excision].
\(^4\)APR OS grouped as lymph node negative/lymph node positive.
\(^5\)Melanoma specific survival.
\(^6\)Mean OS of deceased patients only.

APR: Abdominoperineal resection; WE: Wide excision; mo: Month; OS: Overall survival.
conclusions regarding the benefits of nodal surgery.

Use of immune checkpoint inhibitors and targeted therapies is also controversial and evidence is lacking to help with decision making. While checkpoint inhibitors, tyrosine kinase inhibitors, and BRAF/MEK inhibitors have significantly improved outcomes for cutaneous melanoma over the past decade, their role in treatment of ARM remains unknown\[33-36\]. Results of immune checkpoint inhibitor therapy for ARM are limited and show mixed outcomes. Tokuhara et al\[13\] reported a case of a 67-year-old male with ARM who had no oncologic progression of disease for 17 mo after initiation of anti-programmed death 1 (PD-1) therapy\[13\]. Conversely, Faure et al\[37\] reported a case of a 77 year-old male with ARM who progressed rapidly on anti-PD-1 therapy\[37\]. Higher level evidence of the effectiveness of immune checkpoint inhibitor therapy in treating ARM is lacking\[13,38\]. While immune checkpoint inhibitor therapy has helped individual patients with ARM, the efficacy of this treatment in most ARMs has been questioned as most ARMs do not exhibit 1-PD-ligand expression and few have tumor-infiltrating lymphocytes\[25\]. Evidence for other targeted therapies is similarly poor\[2\]. The genomic profiles of ARMs differ from cutaneous melanomas, with very low BRAF expression and few NRAS and KIT mutations\[39\]. ARM likely has different drivers of metastases with fewer targetable mutations. Although a rare disease, clinical trials are necessary to determine what therapies are most useful for ARM.

This study is limited by its retrospective nature and small cohort size. ARM is an extremely rare disease and only 24 cases were identified over a 20-year period. Additionally, the lack of a synoptic report for this disease has resulted in many
missing pertinent variables which would have strengthened this study.

CONCLUSION

ARM is a highly lethal disease. Over the past 50 years, outcomes have remained largely unchanged. Without good evidence to drive treatment decisions, surgical and non-surgical management remains highly variable across the United States and the world. Even within our own cohort, management differed between patients. Review of the literature was also unable to resolve many questions on ARM. There does not appear to be survival benefit of APR over WE. With no clear advantage to APR, surgical management should aim to minimize morbidity. Many other questions on ARM management remain unanswered. Improving the quality of data on ARM is necessary. A consensus meeting of experts aimed at the identification of pertinent variables to collect would be a good first step. Additionally, clinical trials to assess the role of sentinel lymph node biopsy, targeted therapies, radiation therapy, and treatment sequencing are needed.

ARTICLE HIGHLIGHTS

Research background
Anorectal melanoma (ARM) is a rare disease with poor outcomes. 5-year survival remains < 20%.

Research motivation
Optimal surgical management of ARM remains unknown. Abdominoperineal resection (APR) and wide excision (WE) are both used and no gold standard for primary tumor management currently exists. Understanding trends in management and outcomes is critical to determining appropriate surgical management.

Research objectives
We aimed to update our understanding of treatment outcomes for patients with ARM
and analyze trends across countries and time.

Research methods
We performed a retrospective study of patients who were diagnosed with ARM at 7 hospitals in the Salt Lake City, UT region. We analyzed factors prognostic for recurrence and survival. We also performed a review of the literature to assess regional and temporal trends in ARM management.

Research results
We identified 24 patients diagnosed with ARM between 2000-01 and 2019-05. 12 (50.0%) had local, 8 (33.3%) regional, and 4 (16.7%) distant disease at diagnosis. Only 2 patients who had surgical resection of their primary tumor with curative intent failed to recur. Median time to recurrence was 10.4 mo [interquartile range (IQR) 7.5–17.2] and median overall survival was 18.8 mo (IQR 13.5–33.9). No patients survived to 5 years. No survival differences were noted for patients managed with WE vs APR. Review of the literature demonstrated regional trends in surgical management of ARM, with WE favored in the United States and Europe and APR used more frequently in Asia.

Research conclusions
ARM remains a highly lethal disease regardless of surgical treatment. Patients who undergo WE and APR have poor outcomes. No convincing evidence exists to favor APR over WE. Despite this, APR continues to be used for primary surgical management, although with decreasing frequency in the United States and Europe in recent years. We feel that surgical management should aim to minimize morbidity. WE should be favored over APR for primary surgical treatment.

Research perspectives
Further research should focus on better risk stratification and the role of targeted therapies, radiation therapy, and treatment sequencing. Improving non-surgical therapies will be critical to improving survival for patients with ARM.

ACKNOWLEDGEMENTS
We thank Emily Z. Keung, MD, MD Anderson Cancer Center, Houston, TX, United States.

REFERENCES
1 Chen H, Cai Y, Liu Y, He J, Hu Y, Xiao Q, Hu W, Ding K. Incidence, Surgical Treatment, and Prognosis of Anorectal Melanoma From 1973 to 2011: A Population-Based SEER Analysis. Medicine (Baltimore) 2016; 95: e2770 [PMID: 26886623 DOI: 10.1097/MD.0000000000002770]
2 Paolino G, Didona D, Macri G, Calvieri S, Mercuri SR. Anorectal Melanoma. In: Scott JF, Gerstenblith MR, editors. Noncutaneous Melanoma [Internet]. Brisbane (AU): Codon Publications 2018; 6: 83-98 [PMID: 29874013 DOI: 10.15586/codon.noncutaneousmelanoma.2018.ch6]
3 Patrick RJ, Fenske NA, Messina JL. Primary mucosal melanoma. J Am Acad Dermatol 2007; 56: 828-834 [PMID: 17349716 DOI: 10.1016/j.jaad.2006.06.017]
4 Mihajlovic M, Vlajkovic S, Jovanovic P, Stefanovic V. Primary mucosal melanomas: a comprehensive review. Int J Clin Exp Pathol 2012; 5: 739-753 [PMID: 23071856]
5 van Schaik PM, Ernst MF, Meijer HA, Boschka K. Melanoma of the rectum: a rare entity. World J Gastroenterol 2008; 14: 1633-1635 [PMID: 18330962 DOI: 10.3748/wjg.v14.i16.1632]
6 Khan M, Bucher N, Elhassan A, Barbaryan A, Ali AM, Hussein N, Mirrakhimov AE. Primary anorectal melanoma. Case Rep Oncol 2014; 7: 164-170 [PMID: 24748866 DOI: 10.1159/000360814]
7 Zhang S, Gao F, Wan D. Effect of misdiagnosis on the prognosis of anorectal malignant melanoma. J Cancer Res Clin Oncol 2010; 136: 1401-1405 [PMID: 20130908 DOI: 10.1007/s00432-010-0793-z]
8 National Comprehensive Cancer Network. Cutaneous Melanoma: Clinical Practice Guidelines in Oncology. 2019
9 Choi BM, Kim HR, Yun HR, Choi SH, Cho YB, Kim HC, Yun SH, Lee WY, Chun HK. Treatment outcomes of anorectal melanoma. J Korean Soc Coloproctol 2011; 27: 27-30 [PMID: 21431094 DOI: 10.3393/jsc2011.27.1.27]
10 Kelly P, Zagars GK, Cormier JN, Ross MI, Guadagnolo BA. Sphincter-sparing local excision and hypofractionated radiation therapy for anorectal melanoma: a 20-year experience. Cancer 2011; 117: 4747-4755 [PMID: 21446049 DOI: 10.1002/cncr.26088]
Bleicher J et al. Trends in anorectal melanoma management

11 Ciarrocchi A, Pietroletti R, Carlei F, Amicucci G. Extensive surgery and lymphadenectomy do not improve survival in primary melanoma of the anorectum: results from analysis of a large database (SEER). Colorectal Dis 2017; 19: 158-164 [PMID: 27317493 DOI: 10.1111/col.13412]

12 Taylor JP, Stem M, Yu D, Chen SY, Fang SH, Gearhart SL, Safar B, Efron JE. Treatment Strategies and Survival Trends for Anorectal Melanoma: Is it Time for a Change? World J Surg 2019; 43: 1809-1819 [PMID: 30830243 DOI: 10.1007/s00268-019-04960-w]

13 Tokuhara K, Nakatani K, Tanimura H, Yoshioka K, Kiyohara T, Kon M. A first reported case of metastatic anorectal amelanotic melanoma with a marked response to anti-PD-1 antibody nivolumab: A case report. Int J Surg Case Rep 2017; 31: 188-192 [PMID: 28171845 DOI: 10.1016/j.ijnser.2017.01.028]

14 Knowles J, Lynch AC, Warrier SK, Henderson M, Heriot AG. A case series of anal melanoma including the results of treatment with imatinib in selected patients. Colorectal Dis 2016; 18: 877-882 [PMID: 26546509 DOI: 10.1111/col.12309]

15 Shoushtari AN, Bluth MJ, Goldman DA, Bitas C, Leckowitz RA, Postow MA, Munhoz RR, Buchar G, Hester RH, Romero JA, Fitzpatrick LJ, Weiser MR, Panageas KS, Wolchok JD, Chapman PB, Carvalaj RD. Clinical features and response to systemic therapy in a historical cohort of advanced or unresectable mucosal melanoma. Melanoma Res 2017; 27: 57-64 [PMID: 27792058 DOI: 10.1097/CMR.0000000000000306]

16 Kim KB, Sanguino AM, Hodges C, Papadopoulos NE, Eton O, Camacho LH, Broemeling LD, Johnson MM, Ballo MT, Ross MI, Gershenwald JE, Lee JE, Mansfield PF, Prieto VG, Bedikian AY. Biochemotherapy in patients with metastatic anorectal mucosal melanoma. Cancer 2004; 100: 1478-1483 [PMID: 15042652 DOI: 10.1002/cncr.20113]

17 Liu B, Si L, Cui C, Chi Z, Sheng X, Mao L, Li S, Kong Y, Tang B, Guo J. Phase II randomized trial comparing high-dose IFN-α2b with temozolomide plus cisplatin as systemic adjuvant therapy for resected mucosal melanoma. Clin Cancer Res 2013; 19: 4488-4498 [PMID: 23833309 DOI: 10.1158/1078-0432.CCR-13-0739]

18 PRISMA. Systematic Review and Meta-analysis Checklist. 2009

19 Das G, Gupta S, Shukla PJ, Jagannath P. Anorectal melanoma: a large clinicopathologic study from India. Int Surg 2003; 88: 21-24 [PMID: 12731727]

20 Ranjith S, Muralee M, Sajeed A, Arun PM, Cherran K, Nair CK, Augustine P, Ahamed I. Anorectal melanoma: experience from a tertiary cancer care centre in South India. Ann R Coll Surg Engl 2018; 100: 185-189 [PMID: 29046101 DOI: 10.1016/j.arcse.2017.01.084]

21 Thibault C, Sagar P, Nivatvongs S, Istrup DM, Wolff BG. Anorectal melanoma—an incurable disease? Dis Colon Rectum 1997; 40: 661-668 [PMID: 9194459 DOI: 10.1097/00001436-199706000-00018]

22 Che X, Zhao DB, Wu YK, Wang CF, Cui JQ, Shao YF, Zhao P. Anorectal malignant melanomas: retrospective experience with surgical management. World J Gastroenterol 2011; 17: 534-539 [PMID: 21274385 DOI: 10.3748/wjg.v17.i4.534]

23 Miguel I, Freire J, Passos MJ, Moreira A. Anorectal malignant melanina: retrospective analysis of management and outcome in a single Portuguese Institution. Med Oncol 2015; 32: [445 DOI: 10.1007/s12032-014-0445-3]

24 Ren M, Lu Y, Lv J, Shen X, Kong J, Dai B, Kong Y. Prognostic factors in primary anorectal melanoma: a clinicopathological study of 60 cases in China. Hum Pathol 2018; 79: 77-85 [PMID: 29976316 DOI: 10.1016/j.humpath.2018.05.004]

25 Wanebo HJ, Woodruff JM, Farr GH, Quan SH. Anorectal melanoma. Cancer 1981; 47: 1891-1900 [PMID: 6164474 DOI: 10.1002/1097-0142(19810401)47:7<1891::aid-cncr2820470730>3.0.co;2-k]

26 Yeh JJ, Shia J, Hwu WJ, Busam KJ, Paty PB, Guillem JG, Cott DG, Wong WD, Weiser MR. The role of abdominoperineal resection as surgical therapy for anorectal melanoma. Ann Surg 2006; 244: 1012-1017 [PMID: 17122627 DOI: 10.1097/01.sla.0000225114.56565.f9]

27 Ross M, Pezzi C, Pezzi T, Meurer D, Hickey R, Balch C. Patterns of failure in anorectal melanoma. A guide to surgical therapy. Arch Surg 1990; 125: 313-316 [PMID: 2306178 DOI: 10.1001/archsurg.1990.01410150035007]

28 Hicks CW, Pappou EP, Magruder JT, Gazer B, Fang S, Wick EC, Gearhart SL, Ahuja N, Efron JE. Clinicopathologic Presentation and Natural History of Anorectal Melanoma: A Case Series of 18 Patients. JAMA Surg 2014; 149: 608-611 [PMID: 24848283 DOI: 10.1001/jamasurg.2013.4643]

29 Matsuda A, Miyashita M, Matsumoto S, Takahashi G, Matsutani T, Yamada T, Kishi T, Uchida E. Abdominoperineal resection provides better local control but equivalent overall survival to local excision of anorectal malignant melanoma: a systematic review. Ann Surg 2015; 261: 670-677 [PMID: 25119122 DOI: 10.1097/SLA.0000000000000862]

30 Peterson CV, Garcia-Aguilar J. Abdominoperineal resection for rectal cancer. In: Fischer’s Mastery of Surgery. 2019: 1841-1852

31 Smith HG, Glen J, Turnbull N, Peach H, Board R, Payne M, Gore M, Nugent K, Smith MJF. Less is more: A systematic review and meta-analysis of the outcomes of radical vs conservative primary resection in anorectal melanoma. Eur J Cancer 2020; 135: 113-120 [PMID: 32563895 DOI: 10.1016/j.ejca.2020.04.041]

32 Ishizone S, Koide N, Karasawa F, Akita N, Muranaka F, Ubara H, Miyagawa S. Surgical treatment for anorectal malignant melanoma: report of five cases and review of 79 Japanese cases. Int J Colorectal Dis 2008; 23: 1257-1262 [PMID: 18633625 DOI: 10.1007/s00384-008-0529-6]

33 Freeman M, Laeks S. Surveillance imaging for metastasis in high-risk melanoma: importance in individualized patient care and survivorship. Melanoma Manag 2019; 6: MMT12 [PMID: 31236204]
Bleicher J et al. Trends in anorectal melanoma management

DOI: 10.2217/mmt-2019-0003

34 Joseph RW, Elassaiss-Schaap J, Kefferd R, Huw WJ, Wolchok JD, Joshua AM, Ribas A, Hodi FS, Hamid O, Robert C, Daud A, Dronca R, Hersey P, Weber JS, Patnaik A, de Alwis DP, Perrone A, Zhang J, Kang SP, Ebbinghaus S, Anderson KM, Gangadhar TC. Baseline Tumor Size Is an Independent Prognostic Factor for Overall Survival in Patients with Melanoma Treated with Pembrolizumab. Clin Cancer Res 2018; 24: 4960-4967 [PMID: 29683882 DOI: 10.1158/1078-0432.CCR-17-2336]

35 Long GV, Flaherty KT, Stroyakovskiy D, Gogas H, Levchenko E, de Braud F, Larkin J, Garbe C, Joura T, Hauschild A, Chiarion-Siliéni V, Lebbe C, Mandaå M, Millward M, Arance A, Bondarenko I, Haanen JBAG, Hansson J, Utikal J, Ferraresi V, Mohr P, Probuchai V, Schadendorf D, Nathan P, Robert C, Ribas A, Davies MA, Lane SR, Legos JJ, Mookerjee B, Grob J. dabrafenib plus trametinib in dabrafenib plus trametinib in melanoma patients with metastatic BRAF V600E/K-mutant melanoma: long-term survival and safety analysis of a phase 3 study. Ann Oncol 2017; 28: 1631-1639 [PMID: 28475671 DOI: 10.1093/annonc/mdx176]

36 Kaufman H, Amatruda T, Nemunaitis JJ, Chesney JA, Delman KA, Spitler LE, Collichio FA, Ross MI, Zhang Y, Shilkrut M, Andtbacka RHI. Tumor size and clinical outcomes in melanoma patients (MEL pts) treated with talimogene laherparepvec (T-VEC). J Clin Oncol 2015; 33: 9074 [DOI: 10.1200/jco.2015.33.15_suppl.9074]

37 Faure M, Rochigneux P, Olive D, Taix S, Brenot-Rossi I, Gilabert M. Hyperprogressive Disease in Anorectal Melanoma Treated by PD-1 Inhibitors. Front Immunol 2018; 9: 797 [PMID: 29725330 DOI: 10.3389/fimmu.2018.00797]

38 Cai Y, Cao LC, Zhu CF, Zhao F, Tian BX, Guo SY. Multiple synchronous anorectal melanomas with different colors: A case report. World J Clin Cases 2019; 7: 1337-1343 [PMID: 31236398 DOI: 10.12998/wjcc.v7.i11.1337]

39 Yang HM, Hisiao SJ, Schaeffer DF, Lai C, Remotti HE, Horst D, Mansukhani MM, Horst BA. Identification of recurrent mutational events in anorectal melanoma. Mod Pathol 2017; 30: 286-296 [PMID: 27739435 DOI: 10.1038/modpathol.2016.179]

40 Pack GT, Oropeza R. A comparative study of melanoma and epidermoid carcinoma of the anal canal: A review of 20 melanomas and 29 epidermoid carcinomas (1930 to 1965). Dis Colon Rectum 1967; 10: 161-176 [PMID: 6027697 DOI: 10.1007/BF02617173]

41 Abbas JS, Karakousis CP, Holyoke ED. Anorectal melanoma: clinical features, recurrence and patient survival. Int Surg 1980; 65: 423-426 [PMID: 7451062]

42 Ward MW, Romano G, Nicholls RJ. The surgical treatment of malignant melanoma of the anus. Br J Surg 1986; 73: 68-69 [PMID: 3947881 DOI: 10.1002/bjs.1800730127]

43 Dodos TJ, Wilmotts JS, Jackett LA, Lo SN, Long GV, Thompson JF, Scolyer RA. Primary anorectal melanoma: clinical, immunohistology and DNA analysis of 43 cases. Pathology 2019; 51: 39-45 [PMID: 30497801 DOI: 10.1016/j.pathol.2018.09.060]

44 Siegal B, Cohen D, Jacob ET. Surgical treatment of anorectal melanomas. Am J Surg 1983; 146: 336-338 [PMID: 6614322 DOI: 10.1016/0002-9610(83)90410-5]

45 Roumen RM. Anorectal melanoma in The Netherlands: a report of 63 patients. Eur J Surg Oncol 1996; 22: 598-601 [PMID: 9051514 DOI: 10.1016/0748-798X(96)90234-6]

46 Nilsson P, Ragnarsson-Olding BK. Importance of clear resection margins in anorectal melanoma. Br J Surg 2010; 97: 98-103 [PMID: 20013935 DOI: 10.1002/bjs.6784]

47 Podnos YD, Tsai NC, Smith D, Ellenhorn JD. Factors affecting survival in patients with anal melanoma. Am Surg 2006; 72: 917-920 [PMID: 17058735]

48 Stingluff CL Jr, Vollmer RT, Seigler HF. Anorectal melanoma: clinical characteristics and results of surgical management in twenty-four patients. Surgery 1990; 107: 1-9 [PMID: 2296748]

49 Belli F, Gallino GF, Lo Vullo S, Mariani L, Poiasina E, Leo E. Melanoma of the anorectal region: the experience of the National Cancer Institute of Milano. Eur J Surg Oncol 2009; 35: 757-762 [PMID: 18602790 DOI: 10.1016/j.ejso.2008.05.001]

50 Pessaux P, Pocard M, Elias D, Duviillard P, Avril MF, Zimmerman P, Lasser P. Surgical management of primary anorectal melanoma. Br J Surg 2004; 91: 1183-1187 [PMID: 15449271 DOI: 10.1002/bjs.4592]

51 Ramakrishnan AS, Mahajan V, Kannam R. Optimizing local control in anorectal melanoma. Indian J Cancer 2008; 45: 13-19 [PMID: 18453735 DOI: 10.4103/0019-5099.40641]

52 Homs J, Garrett C. Melanoma of the anal canal: a case series. Dis Colon Rectum 2007; 50: 1004-1010 [PMID: 17468946 DOI: 10.1007/s10350-007-0242-5]

53 Bullard KM, Tuttle TM, Rothenberger DA, Madow RD, Baxter NN, Finne CO, Spencer MP. Surgical therapy for anorectal melanoma. J Am Coll Surg 2003; 196: 206-211 [PMID: 12595048 DOI: 10.1016/S1072-7515(02)01538-7]

54 yen Ch, Chen HH, Chiang SF, Yeh CY, Chen JS, Hsieh PS, Chiang JM, Tsai WS, Tang R, Changchien CR, Wang JY. Anorectal melanoma: review of 22 consecutive cases. Hepatogastroenterology 2013; 60: 89-93 [PMID: 22829553 DOI: 10.5754/htge12453]

55 Aytaç B, Adim SB, Yerci O, Yilmazlar T. Anorectal malignant melanomas: experience of Uludag University. Akhbarisi J Med Sci 2010; 26: 658-662 [PMID: 21186014 DOI: 10.1016/S1607-551X(10)70100-5]

56 Belbaraka R, Elharroudi T, Ismaili N, Fetchoi M, Tijamiyama F, Jalil A, Errihani H. Management of anorectal melanoma: report of 17 cases and literature review. J Gastrointest Cancer 2012; 43: 31-35 [PMID: 20886311 DOI: 10.1007/s10350-010-9216-2]
Nusrath S, Thammineedi SR, Patnaik SC, Raju KV, Pawar S, Goel V, Chavali RN, Murthy S. Anorectal Malignant Melanoma–Defining the Optimal Surgical Treatment and Prognostic Factors. *Indian J Surg Oncol* 2018; 9: 519-523 [PMID: 30538382 DOI: 10.1007/s13193-018-0791-1]

Sahu A, Ramaswamy A, Singhal N, Doshi V, Mirani J, Desouza A, Banavali S, Saklani A, Ostwal V. Metastatic anorectal melanomas - An exploratory retrospective analysis on the benefits of systemic therapy vs best supportive care in a resource-limited setting from India. *South Asian J Cancer* 2017; 6: 147-150 [PMID: 29404289 DOI: 10.4103/sajc.sajc_276_16]
