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CASE REPORT

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Major pathological response after neoadjuvant immunotherapy in esophageal spindle cell carcinoma: A case report

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Abstract

Esophageal spindle cell carcinoma (ESpCC) is a rare subtype of esophageal carcinoma, accounting for 1% of all esophageal malignancies. The clinical outcome is unknown due to the lack of treatment options. Here, we present the case of a 60-year-old male with initially unresectable ESpCC, in which platinum-based concurrent chemoradiotherapy was unsuccessful. He was subsequently treated with neoadjuvant immunotherapy and after surgery achieved a complete pathological response; therefore, neoadjuvant immunotherapy might be a novel option for ESpCC patients.

KEYWORDS

esophageal spindle cell carcinoma, immunotherapy, neoadjuvant treatment

INTRODUCTION

Esophageal cancer is one of the most common gastrointestinal malignancies, affecting millions of people worldwide.[1] Esophageal spindle cell carcinoma (ESpCC) is a rare subtype (about 1%), consisting of a mixture of spindle cells and squamous cells of the same origin.[2–4] ESpCC occurs commonly in males between age of 60–70 years, typically presenting as an intraluminal polypoid mass in the middle of the esophagus.[4–6] The most common symptoms are dysphagia and weight loss, followed by pain.[7, 16]

Optimal treatment of this rare disease is unclear, and it is often treated as poorly differentiated squamous cell carcinoma. Partial or total esophagectomy and lymph node dissection are usually adopted.[4] For locally advanced esophageal cancer, neoadjuvant chemoradiotherapy brings longer event-free survival and overall survival.[8–11] However, this modality remains highly questionable for ESpCC. Few patients have been treated with neoadjuvant or adjuvant therapy in previous studies. Here, we report a patient with locally advanced ESpCC in which treatment with neoadjuvant concurrent chemoradiotherapy failed. He was subsequently treated with neoadjuvant immunotherapy and after surgery achieved a complete pathological response. Neoadjuvant immunotherapy might therefore be a novel option for ESpCC patients.

CASE REPORT

A 60-year-old male came to our hospital with a chief complaint of dysphagia and chest pain for a month. Nodular changes located 23–30 cm from the incisor were visualized by upper endoscopy, involving the whole circumference of the esophageal wall. ESpCC was established by pathological examination, and confirmed by IHC staining (Figure 1) which indicated p63 (+), CK5 / 6 (+), p53 (+), PCK (+), SMA (−), S-100 (−), desmin (−), and Ki-67 (80%). PD-L1 expression was evaluated using the IHC 22C3 pharmDx assay, and a combined positive sore of 40 was assessed. His tumor was judged to be locally advanced (cT3N1M0) through our diagnostic work-up consisting of brain magnetic resonance imaging (MRI), chest and upper abdominal enhanced computed tomography (CT), and bone scintigraphy.

Neoadjuvant chemoradiotherapy was prescribed after consultation with our multidisciplinary team. The chemotherapy regimen consisted nab-paclitaxel plus nedaplatin combination. The dose of thoracic radiotherapy was 4320 cGy/24 F. However, the therapy achieved no efficacy and his tumor remained intact. After discussion, we changed the original

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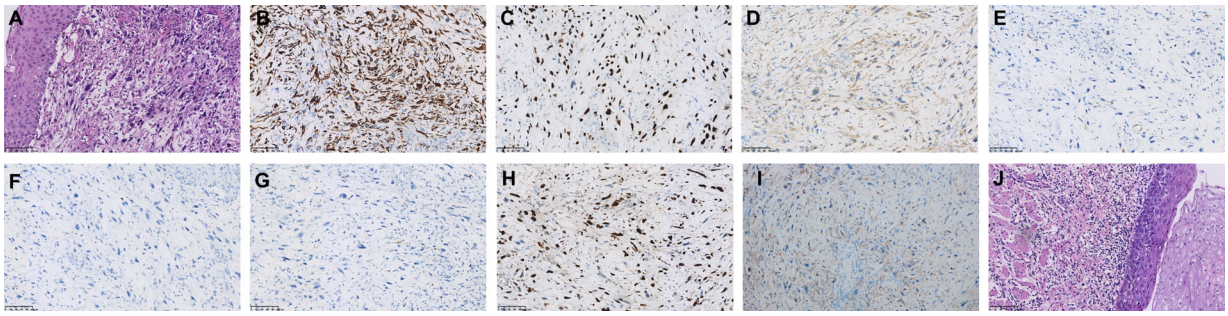

FIGURE 1 Pathological examination showed spindle cell morphology (A: H&E). (B–I) Immunohistochemistry data: CK5/6 (+), P63 (+), PCK (+), SMA (−), desmin (−), s-100(−), ki-67 (+, positive proportion about 80%) and PD-L1(+, positive proportion about 40%), supported the diagnosis. (J) Few tumor cells remained in the postoperative pathological sample. Original magnification, (A–H,J) × 400 and (I) × 200

scheme, and sintilimab (an anti-PD1 antibody, Innovis Inc) at a dose of 200 mg combined with nab-paclitaxel was given every three weeks for two cycles. The lesion markedly decreased in size, and his dysphagia was alleviated (Figure 2).

He finally underwent resection and lymph node dissection of esophageal carcinoma.

Postoperative pathological examination revealed only a few residual tumor cells in the resected tumor sample, with

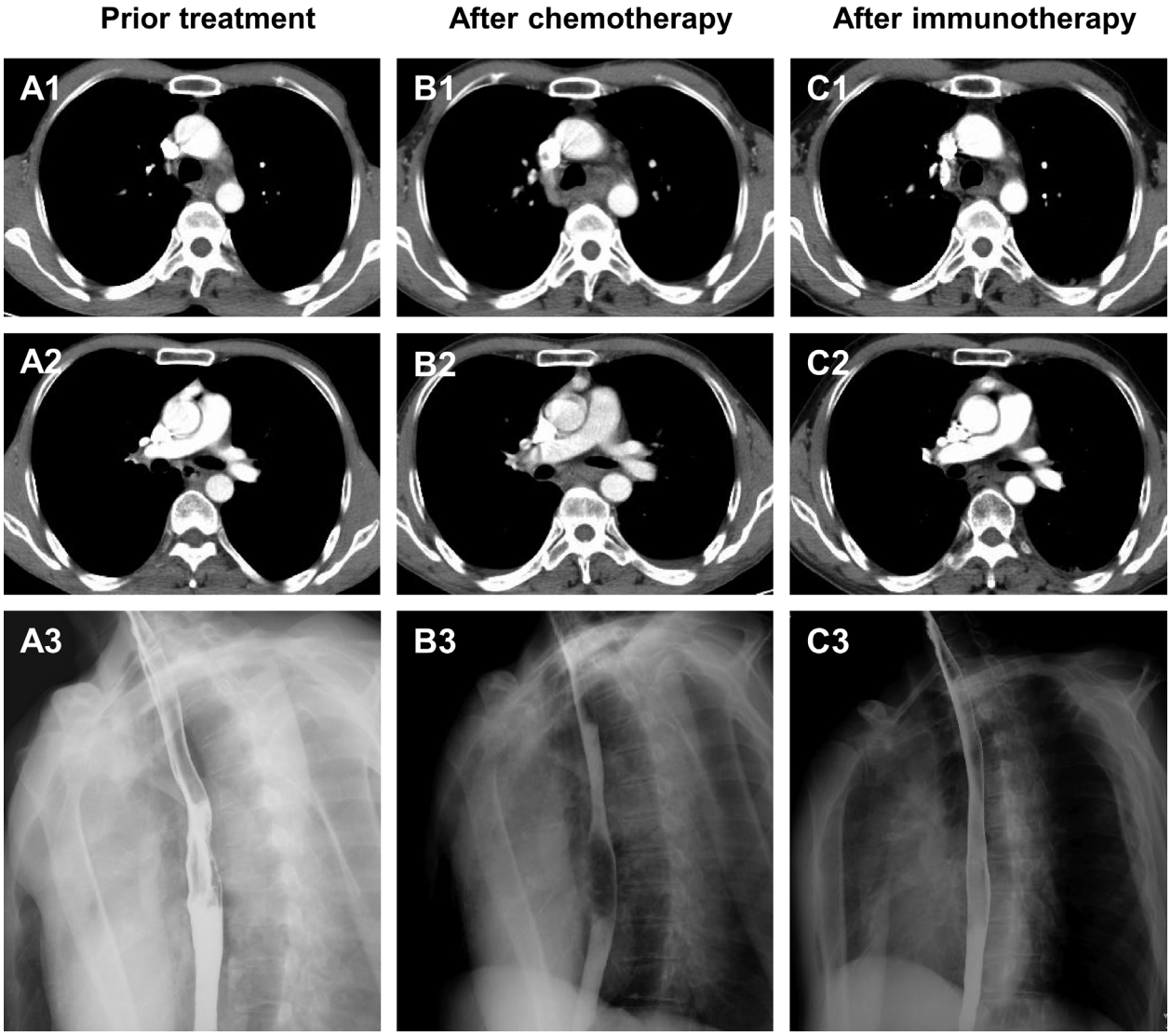

FIGURE 2 Summary of radiological evaluation

TABLE 1 Ongoing immune neoadjuvant trials for esophageal carcinoma

Trial	Phase	Intervention	Population	Patients	Therapy	Primary outcome	Status
NCT04437212	2	Single Group	LA-ESCC	20	Paclitaxel/cisplatin + RT + toripalimab	MPR	Recruiting
NCT02998268	2	Parallel	LA-EAC	46	Pembrolizumab + taxol/carboplatin, surgery, pembrolizumab	DFS	Active
NCT03792347	1b	Single Group	LA-ESCC	20	Carboplatin/paclitaxel + RT + pembrolizumab	Safety	Recruiting
NCT02844075	2	Single Group	LA-ESCC	18	Pembrolizumab + taxol/carboplatin, surgery	pCR	Active
NCT03064490	2	Single Group	LA Gastro/esophageal cancer	38	Pembrolizumab + carboplatin/paclitaxel, surgery, pembrolizumab	pCR	Recruiting
NCT03044613	1b	Single Group	II/III Gastro/esophageal cancer	25	Nivolumab ± relaltimab, carboplatin/paclitaxel + RT, surgery	Safety	Recruiting
NCT03914443	1	Parallel	LA-ESCC	36	Nivolumab + CF or DCF, surgery	Safety	Active
NCT03987815	2	Single Group	Resectable ESCC	20	Nivolumab	MPR	Recruiting
NCT04426955	3	RCT	LA esophageal cancer	390	Camrelizumab + definitive chemoradiotherapy (dCRT) vs. placebo + dCRT	PFS	Recruiting
NCT04506138	2	Single Group	Resectable ESCC	26	Camrelizumab + paclitaxel + carboplatin	pCR,MPR	Recruiting
NCT04225364	2	Single Group	LA-ESCC	50	Camrelizumab + paclitaxel + carboplatin	pCR	Recruiting
NCT03946969	2	Single Group	LA-ESCC	40	Sintilimab + liposomal paclitaxel + cisplatin + S-1	TRAE	Recruiting
NCT03940001	1	Single Group	LA-ESCC	20	Sintilimab + carboplatin/paclitaxel + RT	Unacceptable toxicity, pCR, MPR	Recruiting
NCT04212598	2	Single Group	LA-ESCC	40	Sintilimab + concurrent chemoradiotherapy	DFS, PFS	Recruiting
NCT04548440	2	Single Group	Resectable ESCC	50	Sintilimab + Nab-paclitaxel + cisplatin	R0 resection rate	Recruiting
NCT04006041	2	Single Group	Resectable ESCC	44	Toripalimab + paclitaxel/cisplatin + RT	pCR	Recruiting
NCT04177875	2	Single Group	LA-EC	44	Toripalimab + docetaxel /albumin-bound paclitaxel + cisplatin + RT	MPR, ORR	Recruiting
NCT04177797	2	Single Group	ESCC	20	Toripalimab + paclitaxel + carboplatin	pCR	Recruiting
NCT04280822	3	RCT	Esophageal cancer	400	Toripalimab + paclitaxel + carboplatin	Event-free survival	Recruiting
NCT03087864	2	Single Group	II/III esophageal cancer	40	Atezolizumab + carboplatin + paclitaxel +RT	Percentage completion of treatment	Completed
NCT03448835	2	Single Group	Resectable gastric and EGJ cancer	20	Atezolizumab + capecitabine + oxaliplatin + docetaxel	Safety	Recruiting
NCT02962063	2	Single Group	EAC/EGJ AC	35	Durvalumab + carboplatin + paclitaxel + RT	Unacceptable toxicity, pCR	Recruiting
NCT04221555	2	Parallel	Gastric or EGJ AC	68	Durvalumab + docetaxel + oxaliplatin + S-1, surgery, durvalumab + S-1	pCR	Recruiting
NCT04568200	2	RCT	Resectable ESCC	60	Paclitaxel + carboplatin +RT ± durvalumab	Tumor response pathological response	Recruiting

Abbreviations: CF, 5-FU, CDDP; DCF, 5-FU, CDDP, DTX; DFS, disease-free survival rate; EAC, esophageal adenocarcinoma; EGJ AC, esophagogastric junction adenocarcinoma; ESCC, esophageal squamous cell cancer; LA-EAC, locally advanced esophageal adenocarcinoma; LA-ESCC, locally advanced esophageal squamous cell cancer; MPR, major pathological response; pCR, pathological complete response; RCT, randomized controlled trial; RT, radiotherapy; TRAE, treatment-related adverse events.

scattered lymphocyte infiltration. All the 18 excised lymph nodes were free of tumor cells (ypT1N0M0).

He was maintained on adjuvant sintilimab therapy for another two cycles. Unfortunately, he had gradual onset of exertional dyspnea, and chest CT showed inflammatory infiltration, interstitial involvement, and partial consolidation in bilateral lungs. Immune-related pneumonitis was suspected. After intense methylprednisolone (3 mg/kg) and low dose cyclophophamide (500 mg every week) therapy, the lung lesions gradually resolved. He has survived for 12 months at the time of writing this report.

DISCUSSION

ESpCC has been classified as a special subtype of esophageal squamous cell carcinoma by WHO in 2010.[12] The pathogenesis of ESpCC remains elusive. It is considered to be either a mixed tumor of spindle and squamous cancer cells from a common origin, or a collision of these two kinds of malignant cells from different origins.[2, 7] EspCC exhibits strong immunostaining with cytokeratin AE1/AE3, both in epithelial and spindle compartments. Strong vimentin staining has also been observed in spindle tumor cells. The transitional areas between spindle cell and carcinomatous cells have been previously reported to be positive for both cytokeratin and vimentin.[2, 13–15] The prognosis of ESpCC may be better than that of squamous cell carcinoma. This might be due to its tendency of intraluminal occurrence, and early onset of symptoms.[4, 16]

Our patient received neoadjuvant chemoradiotherapy, which has been shown to improve the prognosis of ESCC. Previously, only one case of ESpCC treated with neoadjuvant therapy has been reported. Neoadjuvant radiotherapy was reported to have an extraordinary objective response in the patient in that study who died after 14 months.[17] Our patient received concurrent chemoradiotherapy as an initial treatment, without noticeable change in tumor size. However, the tumor significantly decreased in size after immunotherapy. Few residual tumor cells were found in postoperative pathology. The treatment process strongly supports the efficacy of immunotherapy in this type of esophageal cancer.

Immunotherapy, including immune checkpoint inhibitors (ICIs), has changed the treatment landscape of esophageal cancer. At least three phase III trials (KEYNOTE-181 for pembrolizumab, ATTRACTION-3 for nivolumab, and ESCORT for camrelizumab) have confirmed the superiority of immunotherapy over chemotherapy in second-line esophageal cancer therapy.[18–20] In a phase III KEYNOTE-590 study, pembrolizumab combined with 5-FU and cisplatin significantly improved OS and PFS in first-line therapy.[21] Perioperative immunotherapy is under active exploration. Checkmate-577 proved the efficacy of adjuvant nivolumab for patients undergoing concurrent chemoradiotherapy for neoadjuvant.[22] A dozen neoadjuvant immunotherapy clinical trials are ongoing (Table 1).

ESpCC is also referred to as esophageal sarcomatoid carcinoma (SC). Studies in SC of other sites might lend meaningful references to the largely-unknown treatment of ESpCC. SC is usually an extremely malignant tumor with a poor outcome which has previously been reported to be resistant to chemotherapy or radiotherapy.[23] Yvorel et al. measured PD-L1 (defined as >10%) that was expressed in 75% (27/36) of pulmonary SC patients.[28] In another report, a PD-L1 expression rate of 53% (40/75) in pulmonary SC patients was reported, higher than other subtypes of NSCLC.[27] High expression rates of PD-L1 in kidney SC have also been observed.[29, 30] High tumor mutation burden (TMB) has been reported to be more common in pulmonary SC than other types of NSCLC. In the report by Alexa et al., where high TMB was defined as >20/Mb, the proportions of high TMB were 20% and 14%, respectively.[31] In another report, high TMB (>10/Mb) was observed in 87.5% (7/8) of PSC patients.[32] In addition, at least one article has reported the high density of CD8+ tumor infiltrating lymphocytes in the microenvironment of sarcomatoid renal cell carcinoma (SRCC).[29] It is generally believed the expression of PD-L1 and TMB are positively correlated with immunotherapy.[24–26] Therefore, the prospect of PD-1/ PD-L1 inhibitors for the treatment of SC seems promising. This has been confirmed by retrospective studies and also anecdotal case reports on pulmonary SC and SRCC.[33–35]

Recently, the combination of durvalumab (an anti-PD-L1 antibody) plus tremelimumab (an anti-CTLA4 antibody) in the treatment of pulmonary SC was tested in a prospective single-arm phase 2 trial (KCSG-LU16-07). The results showed that PFS, OS, ORR and DCR were 5.9 m, 15.4 m, 26.7% and 60%, respectively.[36] In four phase 3 trials (Keynote-426, CheckMate-214, IMmotion151 and JAVELIN Renal 101), pembrolizumab, nivolumab, atezolizumab and avelumab were shown to bring survival benefit to SRCC in subgroup analyses.[30, 37–40] All these studies suggest that there are potential benefits of immunotherapy for SC, which might be helpful in the treatment of ESpCC.

In conclusion, in this report we described a case of esophageal carcinosarcoma treated with neoadjuvant immunotherapy after failure of preoperative chemoradiotherapy. Immunotherapy might therefore be a useful candidate for patients with locally advanced ESpCC.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424. https://doi.org/10.3322/caac.21492.
2. Raza MA, Mazzara PF. Sarcomatoid carcinoma of esophagus. Arch Pathol Lab Med. 2011;135(7):945–8. https://doi.org/10.1043/2010-0074-RSR.1.

3. Iwaya T, Maesawa C, Tamura G, Sato N, Ikeda K, Sasaki A, et al. Esophageal carcinosarcoma: A genetic analysis. Gastroenterology. 1997;113:973–7. https://doi.org/10.1016/s0016-5085(97)70194-x.
4. Zhang B, Xiao Q, Yang D, Li X, Hu J, Wang Y, et al. Spindle cell carcinoma of the esophagus: A multicenter analysis in comparison with typical squamous cell carcinoma. Medicine (Baltimore). 2016;95:e4768 https://doi.org/10.1097/MD.0000000000004768.
5. Kwon MS, Hong SJ, Cho HA, Ahn GH, Lee SS, Lee KY, et al. Extensive and divergent chromosomal losses in squamous and spindle-cell components of esophageal sarcomatoid carcinoma. Virchows Arch. 2003;443:635–42. https://doi.org/10.1007/s00428-003-0873-4.
6. Sanada Y, Hihara J, Yoshida K, Yamaguchi Y. Esophageal carcinosarcoma with intramural metastasis. Dis Esophagus. 2006;19:119–31. https://doi.org/10.1111/j.1442-2050.2006.00551.x.
7. Iascone C, Barreca M. Carcinosarcoma and pseudosarcoma of the esophagus: Two names, one disease–Comprehensive review of the literature. World J Surg. 1999;23:153–7. https://doi.org/10.1007/pl00013169.
8. Yang H, Liu H, Chen Y, Zhu C, Fang W, Yu Z, et al. Neoadjuvant chemoradiotherapy followed by surgery versus surgery alone for locally advanced squamous cell carcinoma of the esophagus (NEOCRTEC5010): A phase III multicenter, randomized, open-label clinical trial. J Clin Oncol. 2018;36:2796–803. https://doi.org/10.1200/JCO.2018.79.1483.
9. Sjoquist KM, Burmeister BH, Smithers BM, Zalcberg JR, Simes RJ, Barbour A, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: An updated meta-analysis. Lancet Oncol. 2011;12:681–92. https://doi.org/10.1016/S1470-2045(11)70142-5.
10. Burmeister BH, Smithers BM, Gebski V, Fitzgerald L, Simes RJ, Devitt P, et al. Surgery alone versus chemoradiotherapy followed by surgery for resectable cancer of the oesophagus: A randomised controlled phase III trial. Lancet Oncol. 2005;6:659–68. https://doi.org/10.1016/S1470-2045(05)70288-6.
11. Shapiro J, van Lanschot JJB, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, Wijnhover BPL, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): Long-term results of a randomised controlled trial. Lancet Oncol. 2015;16:1090–8. https://doi.org/10.1016/S1470-2045(15)00040-6.
12. Bosman FT, Carneiro F, Hruban RH, Theise N. WHO Classifcation of Tumor of the Digestive Tumors. Vol 3. 4th ed. Lyon: International Agency for Research on Cancer; 2010.p. 15–44.
13. Guarino M, Tricomi P, Giordano F, Cristofori E. Sarcomatoid carcinomas: Pathological and histopathogenetic considerations. Pathology. 1996;28:298–305. https://doi.org/10.1080/00313029600169224.
14. Wang ZY, Itabashi M, Hirota T, Watanabe H, Kato H. Immunohistochemical study of the histogenesis of esophageal carcinosarcoma. Jpn J Clin Oncol. 1992;22:377–86.
15. Hashimoto M, Kitagami H, Niwa H, Kikkawa T, Ohuchi T, Takenouchi T, et al. Prognosis and prognostic factors of esophageal spindle cell carcinoma treated by esophagectomy: A retrospective single-institution analysis. Esophagus. 2019;16:292–9. https://doi.org/10.1007/s10388-019-00667-y.
16. Wang L, Lin Y, Long H, Liu H, Rao H, He Y, et al. Esophageal carcinosarcoma: A unique entity with better prognosis. Ann Surg Oncol. 2013;20:997–1004. https://doi.org/10.1245/s10434-012-2658-y.
17. Ogasawara N, Tamura Y, Funaki Y, Yamaguchi Y, Shimozato A, Yanamoto K, et al. Rapidly growing esophageal carcinosarcoma reduced by neoadjuvant radiotherapy alone. Case Rep Gastroenterol. 2014;8:227–34. https://doi.org/10.1159/000365320.
18. Kojima T, Shah MA, Muro K, Francois E, Adenis A, Hsu C-H, et al. Randomized phase III KEYNOTE-181 study of Pembrolizumab versus chemotherapy in advanced esophageal cancer. J Clin Oncol. 2020;38:4138–48. https://doi.org/10.1200/JCO.20.01888.
19. Kato K, Cho BC, Takahashi M, Okada M, Lin C-Y, Chin K, et al. Nivolumab versus chemotherapy in patients with advanced oesophageal squamous cell carcinoma refractory or intolerant to previous chemotherapy (ATTRACTION-3): A multicentre, randomised, open-label, phase 3 trial. Lancet Oncol. 2019;20:1506–17. https://doi.org/10.1016/S1470-2045(19)30626-6.
20. Huang J, Xu J, Chen Y, Zhuang W, Zhang Y, Chen Z, et al. Camrelizumab versus investigator's choice of chemotherapy as second-line therapy for advanced or metastatic oesophageal squamous cell carcinoma (ESCORT): A multicentre, randomised, open-label, phase 3 study. Lancet Oncol. 2020;21:832–42. https://doi.org/10.1016/S1470-2045(20)30110-8.
21. Merck's Keytruda (pembrolizumab) in combination with chemotherapy significantly improved overall survival and progression-free survival compared with chemotherapy in locally advanced or first-line metastatic esophageal cancer [news release]. Kenilworth, NJ. Published august 19, 2020. [cited 2020 Aug 19]. Available from: https://www.merck.com/news/mercks-keytruda-pembrolizumab-in-combination-with-chemotherapy-significantly-improved-overall-survival-and-progression-free-survival-compared-with-chemotherapy-in-locally-advanced-or/.
22. Kelly RJ, Ajani JA, Kuzdzal J, Zander T, van Cutsem E, Piessen G, et al. Adjuvant nivoluamb in resected esophageal or gastroesophageal junction cancer (EC/GEJC) following neoadjuvant chemoradiation therapy (CRT): First results of the CheckMate 577 study. Ann Oncol; 31(Suppl 4):S1142–S1215. https://doi.org/10.1016/annonc/annonc325.
23. Vieira T, Girard N, Ung M, Monnet I, Cazes A, Bonnette P, et al. Efficacy of first-line chemotherapy in patients with advanced lung sarcomatoid carcinoma. J Thorac Oncol. 2013;8:1574–7. https://doi.org/10.1097/01.JTO.0000437008.00554.90.
24. Reck M, Rodríguez-Abreu D, Robinson AG, Hui R, Csőszi T, Fülöp A, et al. Pembrolizumab versus chemotherapy for PD-L1-Positive Non-Small-Cell lung Cancer. N Engl J Med. 2016;375:1823–33. https://doi.org/10.1056/NEJMoa1606774.
25. Mok TSK, Wu YL, Kudaba I, Kowalski DM, Cho BC, Turna HZ, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): A randomised, open-label, controlled, phase 3 trial. Lancet. 2019;393:1819–30. https://doi.org/10.1016/S0140-6736(18)32409-7.
26. Marabelle A, Fakih M, Lopez J, Shah M, Shapira-Frommer R, Nakagawa K, et al. Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: Prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. Lancet Oncol. 2020;21:1353–65. https://doi.org/10.1016/S1470-2045(20)30445-9.
27. Vieira T, Antoine M, Hamard C, Fallet V, Duruisseaux M, Rabbe N, et al. Sarcomatoid lung carcinomas show high levels of programmed death ligand-1 (PD-L1) and strong immune-cell infiltration by TCD3 cells and macrophages. Lung Cancer. 2016;98:51–8. https://doi.org/10.1016/j.lungcan.2016.05.013.
28. Yvorel V, Patoir A, Casteillo F, Tissot C, Fournel P, Stachowicz ML, et al. PD-L1 expression in pleomorphic, spindle cell and giant cell carcinoma of the lung is related to TTF-1, p40 expression and might indicate a worse prognosis. PLoS One. 2017;12:e0180346 https://doi.org/10.1371/journal.pone.0180346.
29. Debien V, Thouvenin J, Lindner V, Barthélémy P, Lang H, Flippot R, et al. Sarcomatoid dedifferentiation in renal cell carcinoma: From novel molecular insights to new clinical opportunities. Cancers (Basel). 2019;12(1). https://doi.org/10.3390/cancers12010099.
30. Iacovelli R, Ciccarese C, Bria E, Bracarda S, Porta C, Procopio G, et al. Patients with sarcomatoid renal cell carcinoma - re-defining the first-line of treatment: A meta-analysis of randomised clinical trials with immune checkpoint inhibitors. Eur J Cancer. 2020;136:195–203. https://doi.org/10.1016/j.ejca.2020.06.008.
31. Schrock AB, Li SD, Frampton GM, Suh J, Braun E, Mehra R, et al. Pulmonary sarcomatoid carcinomas commonly harbor either potentially targetable genomic alterations or high tumor mutational burden as observed by comprehensive genomic profiling. J Thorac Oncol. 2017;12:932–42. https://doi.org/10.1016/j.jtho.2017.03.005.
32. Domblides C, Leroy K, Monnet I, Mazières J, Barlesi F, Gounant V, et al. Efficacy of immune checkpoint inhibitors in lung sarcomatoid

carcinoma. J Thorac Oncol. 2020;15:860–6. https://doi.org/10.1016/j.jtho.2020.01.014.
33. Gounant V, Brosseau S, Naltet C, Opsomer MA, Antoine M, Danel C, et al. Nivolumab-induced organizing pneumonitis in a patient with lung sarcomatoid carcinoma. Lung Cancer. 2016;99:162–5. https://doi.org/10.1016/j.lungcan.2016.07.010.
34. Mayenga M, Assié JB, Monnet I, Massiani MA, Tabeze L, Friard S, et al. Durable responses to immunotherapy of non-small cell lung cancers harboring MET exon-14-skipping mutation: A series of 6 case. Lung Cancer. 2020;150:21–5. https://doi.org/10.1016/j.lungcan.2020.09.008.
35. Hanif A, Pandey M, Khan S, Attwood K, George S. Metastatic sarcomatoid renal cell carcinoma treated with immune checkpoint inhibitors. Onco Targets Ther. 2019;8:1606639. https://doi.org/10.1080/2162402X.2019.1606639.
36. Kim M, Keam B, Ock CY, Kim SH, Kim YJ, Lim SM, et al. Phase II study of durvalumab and tremelimumab in pulmonary sarcomatoid carcinoma: KCSG-LU16-07. Thorac Cancer. 2020;11:3482–9. https://doi.org/10.1111/1759-7714.13684.
37. Rini BI, Plimack ER, Stus V, Gafanov R, Hawkins R, Nosov D, et al. Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for metastatic renal cell carcinoma (mRCC): Outcomes in the combined IMDC intermediate/poor risk and sarcomatoid subgroups of the phase 3 KEYNOTE-426 study. J Clin Oncol. 2019;37:(suppl; abstr 4500).
38. McDermott DF, Choueiri TK, Motzer RJ, Aren OR, George S, Powles T, et al. CheckMate 214 post-hoc analyses of nivolumab plus ipilimumab or sunitinib in IMDC intermediate/poor-risk patients with previously untreated advanced renal cell carcinoma with sarcomatoid features. J Clin Oncol. 2019;37: (suppl; abstr 4513).
39. Rini BI, Motzer RJ, Powles T, McDermott DF, Escudier B, Donskov F, et al. Atezolizumab (atezo) +bevacizumab (bev) versus sunitinib (sun) in pts with untreated metastatic renal cell carcinoma (mRCC) and sarcomatoid (sarc) histology: IMmotion151 subgroup analysis. J Clin Oncol. 2019;37(15 suppl):4512–2. https://doi.org/10.1200/JCO.2019.37.15_suppl.4512.
40. Choueiri TK, Larkin JMG, Pal SK, Motzer RJ, Venugopal B, Alekseev BY, et al. Efficacy and biomarker analysis of patients (pts) with advanced renal cell carcinoma (aRCC) with sarcomatoid histology (sRCC): Subgroup analysis from the phase 3 JAVELIN renal 101 trial of first-line avelumab plus axitinib (A þ Ax) vs sunitinib (S). Ann Oncol. 2019;30(suppl5):v356e402 https://doi.org/10.1093/annonc/mdz249.

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