Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with metastatic oesophageal cancer: a JSMO–ESMO initiative endorsed by CSCO, KSMO, MOS, SSO and TOS


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The most recent version of the European Society for Medical Oncology (ESMO) Clinical Practice Guidelines for the diagnosis, treatment and follow-up of oesophageal cancer was published in 2016, and covered the management and treatment of local/locoregional disease, limited disease, locally advanced disease and the management of advanced/metastatic disease. At the ESMO Asia Meeting in November 2017 it was decided by both ESMO and the Japanese Society of Medical Oncology (JSMO) to convene a special guidelines meeting immediately after the JSMO Annual Meeting in 2018. The aim was to adapt the ESMO 2016 guidelines to take into account the ethnic differences associated with the treatment of metastatic oesophageal cancer in Asian patients. These guidelines represent the consensus opinions reached by experts in the treatment of patients with metastatic oesophageal cancer representing the oncological societies of Japan (JSMO), China (CSCO), Korea (KSMO), Malaysia (MOS), Singapore (SSO) and Taiwan (TOS). The voting was based on scientific evidence, and was independent of both the current treatment practices and the drug availability and reimbursement situations in the individual participating Asian countries.

Key words: metastatic oesophageal cancer, Pan-Asian, consensus, guidelines
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Introduction

Oesophageal cancer was the eighth most common cancer worldwide and the sixth most common cause of death from cancer in 2012, with an estimated 456,000 new cases (3.2% of the total cancer cases) and an estimated 400,000 deaths (4.9% of the total cancer deaths) recorded [1]. There are two main histological types of oesophageal cancer, oesophageal squamous cell carcinoma (SCC) and oesophageal adenocarcinoma and these figures include both of these subtypes. Oesophageal cancer is rare in young people with most patients presenting in their 70s and 80s.

Around 80% of the cases worldwide occur in less developed regions with global incidence rates threefold higher in men than in women. For both sexes, there are more than 20-fold differences in incidence between geographical regions, with rates (per 100,000) ranging from 0.8 in Western Africa to 17.0 in Eastern Asia in men, and 0.2 in Micronesia/Ponies to 7.8 in Eastern Africa in women. Furthermore, the regional mortality rates closely follow the regional incidence rates as illustrated by the high mortality rate, 14.1 per 100,000, seen for men in Eastern Asia. The regional variations in the incidences and type of oesophageal cancer are driven by differences in risk factors, although for some regions these are not fully understood [2]. SCCs account for 90% of oesophageal cancers worldwide and are more common in the regions with the highest incidence rates for oesophageal cancer, whilst adenocarcinomas are most common in the regions with the lowest incidence rates. Also, while the incidence of SCCs is decreasing in Europe and North America [3], the incidence of oesophageal adenocarcinomas has been increasing in North America and Western countries such as Australia, France and England, and is postulated to be due to the increasing obesity of their populations and the associated increase of gastroesophageal reflux and Barret’s oesophagus [4]. Helicobacter pylori (H. pylori) infection and CagA-positive strains are associated with a decreased risk of oesophageal adenocarcinoma.

Guidelines for the diagnosis and treatment of oesophageal cancer and an evaluation of the effectiveness of screening for oesophageal cancer have recently been published in Japan [5, 6] and China [7], respectively. The ESMO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of oesophageal cancer have also recently been published [8], and a decision was taken by the ESMO and JSMO to use these ESMO guidelines to develop guidelines for the treatment and management of Asian patients with metastatic oesophageal cancer. A 1-day working meeting was held on the 22 July 2018 in Kobe Japan immediately after the 16th Annual Meeting of the JSMO, for this purpose. Finalisation of the Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with metastatic gastric cancer took place at the same meeting and will be published separately [9].

Methodology

This Pan-Asian adaptation of the ESMO guidelines was prepared in accordance with the processes and format developed for the preparation of the first Pan-Asian adapted ESMO consensus guidelines for the management of patients with metastatic colorectal cancer [10].

Composition of expert panel

The international panel of experts was selected according to their demonstrable knowledge of the field of gastric and oesophageal cancer patient treatment and management in terms of publications and/or their participation in the development of national or international treatment guidelines. More specifically, this included 10 expert members of the JSMO, 8 expert members from the ESMO and 2 experts each from the oncological societies of China (CSCO), Korea (KMSO), Malaysia (MOS), Singapore (SSO) and Taiwan (TOS). Only 2 of the 10 expert members from the JSMO (EB and KK) were allowed to vote on the recommendations together with the 2 experts from each of the 5 other Asian oncological societies.

Provisional statements

A set of preformulated topics and five categories of recommendations for the treatment of metastatic oesophageal cancer based on those in the latest ESMO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of oesophageal cancer were circulated before the meeting to each of the 12 Asian experts selected to represent the 6 Asian oncological societies to gather their comments on each of the recommendations. As described previously for the Pan-Asian adaptation of the ESMO guidelines for metastatic gastric cancer, the Asian experts were specifically asked ‘Is this recommendation adaptable for use in your country?’ The 12 experts were also asked to provide details of the reasoning behind their responses and the relevant references to support their decisions.

Voting process

A modified Delphi process was used to develop each individual statement before the final discussion and the voting process at the face-to-face working meeting in Kobe. The 12 Asian experts were asked to vote based on the evidence available, on a scale of A to E, where A = accept completely; B = accept with some reservation; C = accept with major reservation; D = reject with some reservation and E = reject completely (Table 1). An adapted version of the Infectious Diseases Society of America–United States Public Health Service Grading System [11] was used to define the level of evidence and strength of each recommendation proposed by the group, as for all of the ESMO Consensus and ESMO Clinical Practice Guidelines (Table 1), and are given in the text in square brackets after each recommendation together with details of the levels of agreement. Most statements on the level of agreement were based on peer-reviewed manuscript data, although statements made based on expert opinion were also considered to be justified standard clinical practice by the experts and the JSMO and ESMO faculty. The remaining 16 experts, 8 from the JSMO and eight from the ESMO were present at the face-to-face meeting to offer expert opinion if and as required, with one
non-voting member of the JSMO (KM) and one non-voting member of the ESMO (FL) co-chairing the meeting.

Final consensus statements

A consensus was considered to have been achieved when ≥80% of experts voted to accept completely or accept with reservation a specific recommendation as described previously for the Pan-Asian adaptation of the ESMO gastric cancer guidelines.

Results

In the initial pre-meeting survey, experts representing six Asian countries (Japan, China, Korea, Malaysia, Singapore and Taiwan) reported on the applicability of the recommendations for the treatment of metastatic oesophageal cancer from the 2016 ESMO Clinical Practice Guidelines [8]. These recommendations were made in the categories:

1. Biomarkers
2. Diagnosis and pathology (2a and b)
3. Stage and risk assessment (3a, b, c, d and e)
4. Management of advanced disease (4a, b and c)
5. Personalised medicine (5a and b)

and for the purposes of the evaluation and voting process were numbered recommendations 1 to 5 with the subcategories assigned a letter code (a, b, c etc.). An unqualified response of YES in the pre-meeting survey equated with ‘accept completely’ in the final voting, i.e. A = 100%. These recommendations were restricted to consideration of metastatic oesophageal cancer only, due to the complexity of modifying the European recommendations for the treatment and management of localised oesophageal cancer in Asian patients. The treatment approaches for patients with localised NSCLC vary considerably between Asia and Europe. Following the initial survey, agreement was not reached between countries on recommendations 3a, b, c, d and e, 4a and c and 5a (supplementary Table S1, available at Annals of Oncology online). At the face-to-face meeting in Kobe, the 12 Asian experts in the treatment of oesophageal cancer were asked to discuss and to vote again on these recommendations. Voting again on recommendations 1, and 2 was not necessary. The final levels of agreement and levels of evidence together with, where appropriate, a description of the strength of support recorded for each ESMO recommendation by the Asian panel members are provided in the text below beside each of the 5 recommendations and their subcategories as appropriate. Where changes to the original text have been made, these are emphasised in bold text both in the main text of the manuscript and in Table 2, and reference made to the change in the text as appropriate. In parallel, the final voting patterns of the representatives of each of the participating regions for the ESMO recommendations are presented in supplementary Table S2, available at Annals of Oncology online.

Recommendation 1: biomarkers

1. **Immunohistochemistry for HER2 protein expression or (fluorescence) in situ hybridisation to assess HER2 gene amplification should be used to select patients with metastatic oesophageal adenocarcinoma for treatment with a trastuzumab-containing regimen [A = 100% and I, A].**

All 12 Asian experts accepted completely [A = 100%] ‘recommendation 1’ above that the human epidermal growth factor receptor-2 (HER2) status (HER2 positivity) of the tumours of all patients with adenocarcinomas of the oesophagus or
gastroesophageal junction (GEJ) should be established at the time of diagnosis using the same methods as those used in patients diagnosed with gastric cancer. This was based on the results of the phase III ToGA trial in which trastuzumab in combination with capcitabine and cisplatin was shown to be more effective than chemotherapy alone in patients with HER2-positive advanced GEJ cancer (18% of patients) [12]. Subgroup analysis of Asian patients included in the ToGA trial confirmed these results [13]. Trastuzumab is recommended in combination with chemotherapy for the treatment of patients with HER2 immunohistochemistry (IHC) 2+ with fluorescence in situ hybridisation (FISH)-positive or IHC 3+ adenocarcinomas.

**Recommendation 2: diagnosis and pathology**

2a. All patients with new dysphagia, gastrointestinal bleeding, recurrent aspiration or emesis, weight loss and/or loss of appetite should undergo an upper intestinal endoscopy [A = 100% and III, A].

2b. Immunohistochemical staining is recommended in poorly and undifferentiated cancers (Grade 3 or 4) according to the WHO to differentiate between SCC and adenocarcinoma of the oesophagus [A = 100 and V, B].

All 12 Asian experts accepted completely [A = 100%] ‘recommendations 2a and 2b’ above. Dysphagia, gastrointestinal bleeding, recurrent aspiration or emesis, weight loss and are/or loss of appetite are all important symptoms of oesophageal cancer, thus all patients with such symptoms should undergo upper intestinal endoscopy. As reported in the previous guidelines [8], approximately three quarters of oesophageal adenocarcinomas are found in the distal oesophagus, whilst oesophageal SCCs are found more frequently in the proximal to middle oesophagus [14]. Diagnosis should be made from endoscopic biopsies taken from all suspect areas and the histology classified according the World Health Organization (WHO) criteria [15]. However, in Japan, oesophageal cancer is diagnosed histologically according to the Japanese Classification of Oesophageal Cancer. Immunohistochemical staining is recommended in poorly and undifferentiated cancers [9].

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**Table 2. Summary of Asian recommendations for patients with metastatic oesophageal cancer**

<table>
<thead>
<tr>
<th>Recommendation 1: biomarkers</th>
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<tbody>
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<th>Recommendation 3: staging and risk assessment</th>
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<tr>
<td>3a. Decisions on the initial treatment approach of oesophageal cancer are taken on the basis of clinical staging, which should be carried out with the highest degree of accuracy possible. Staging should include a complete clinical examination and a CT scan of the neck, chest and abdomen [A = 100% and III, A].</td>
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<tr>
<td>3b. 18F-FDG-PET should be carried out in patients who are candidates for oesophagectomy [A = 100% and III, B].</td>
</tr>
<tr>
<td>3c. In the case of oesophageal SCC due to chronic tobacco and alcohol consumption consideration should be given to investigation for the presence of a second primary cancers of the aerodigestive tract [A = 100% and IVB].</td>
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<tr>
<td>3d. Nutritional support is an integral part of the medical care for patients with oesophageal cancer in the curative and palliative settings. Patient nutritional status and history of weight loss should be assessed according to national or international guidelines [A = 100% and III, A].</td>
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<th>Recommendation 4: management of advanced disease</th>
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<tr>
<td>4a. Patients with metastatic oesophageal cancer can be considered for different palliative treatment options depending on the clinical situation.</td>
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<tr>
<td>4b. Chemotherapy is indicated for palliative treatment in selected patients, particularly for patients with adenocarcinoma who have a good performance status [A = 100% and IIIB].</td>
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<tr>
<td>4c. In squamous cell oesophageal cancer, combination chemotherapy is the preferred option in clinical practice for fit patients [A = 100%]. BSC or palliative monotherapy should be considered for unfit patients [A = 100% and IIB].</td>
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<th>Recommendation 5: personalised medicine</th>
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<tr>
<td>5a. Trastuzumab–containing treatment is recommended for HER2-positive GEJ adenocarcinomas. It is an option for patients with HER2-positive pure oesophageal adenocarcinomas despite their rarity [A = 100% and I, A].</td>
</tr>
</tbody>
</table>

BSC, best supportive care; CT, computed tomography; 18F-FDG-PET, 18F-fluoro-2-deoxy-D-glucose positron emission tomography; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor-2; SCC, squamous cell carcinoma; WHO, World Health Organization.
cancers (grade 3 or 4) to differentiate between SCCs and adenocarcinomas. Differentiating between these two histological subtypes has both prognostic and clinical significance. In addition to these two histological subtypes, small cell carcinomas and other rare histological subtypes such as endocrine tumours, lymphomas, mesenchymal tumours and melanoma need to be identified histologically [8].

### Recommendation 3: stage and risk assessment

3a. **Decisions on the initial treatment approach of oesophageal cancer are taken on the basis of clinical staging, which should be carried out with the highest degree of accuracy possible. Staging should include a complete clinical examination and a computed tomography (CT) scan of the neck, chest and abdomen [A = 100% and III, A].**

3b.1. **18F-Fluoro-2-deoxy-D-glucose (FDG)-positron emission tomography (PET) should be carried out in patients who are candidates for oesophagectomy [A = 100% and III, B].**

3b.2. **18F-FDG-PET should not routinely be recommended for patients with known metastatic disease [A = 100% and III, B].**

3c. **In the case of oesophageal SCC due to chronic tobacco and alcohol consumption, meticulous investigation of the oral cavity, oropharynx and hypopharynx by an ear, nose and throat specialist, as well as trachea-bronchoscopy to exclude synchronous second cancers in the aerodigestive tract, should be carried out [IV, B], was revised to read ‘In the case of oesophageal SCC due to chronic tobacco and alcohol consumption consideration should be given to investigation for the presence of second primary cancers of the aerodigestive tract [A = 100% and IV, B]’.**

3d. **The nutritional status and history of weight loss should be assessed according to the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines, was revised and merged with recommendation 3e below to become part of the new revised ‘recommendation 3d’ in bold text below.**

3e. **Nutritional support according to the ESPEN guidelines is an integral part of the medical care for patients with oesophageal cancer in the curative and in the palliative setting, was revised and merged with the original recommendation 3d above to become part of the new revised ‘recommendation 3d’ in bold text below.**

3d. **Nutritional support is an integral part of the medical care for patients with oesophageal cancer in the curative and palliative settings. Patient nutritional status and history of weight loss should be assessed according to national or international guidelines [A = 100% and III, A].**

All 12 Asian experts accepted completely [A = 100%] ‘recommendation 3a’ after discussion, and ‘recommendation 3b’ was accepted completely [A = 100%] and accepted completely [A = 83%] or with some reservation [B = 17%] after it was revised to become ‘recommendations 3b-1 and 3b-2’ above (supplementary Table S2, available at *Annals of Oncology* online). The first part of the original ‘recommendation 3b’ was deleted because it referred to the early-stage disease situation. There are no Pan-Asian or country-specific guidelines on the use of either CT scans for clinical staging or the use of endoscopic ultrasound (EUS) and 18F-FDG-PET in patients who are candidates for surgery. In Asia, all physicians request CT scans of the chest but CT scans of the neck and abdomen can be at the request of the treating physician. Metastasis to the lymph nodes is a key determinant of prognosis for patients with oesophageal SCC [16, 17]. Twenty to fifty percent of patients with oesophageal SCCs are diagnosed with cervical lymph node metastasis and Chinese data (n = 1850) showed that 26.5% of patients developed abdominal lymph node metastasis [18]. The liver is also one of the most common sites of metastasis. All the Asian experts agreed completely [A = 100%] that CT scans of the neck, chest and abdomen are required to develop the appropriate treatment plans for Asian patients with oesophageal SCCs. In the case of patients with adenocarcinomas of the oesophagus or GEJ, abdominal lymph node metastases are reported in more than 10% of patients [19, 20]. The liver is also one of the most common sites of metastasis. However, given that cervical oesophageal adenocarcinoma is extremely rare the experts agreed that only CT scans of the chest and abdomen are required to inform the treatment of patients with oesophageal adenocarcinoma. However, EUS has been shown to be superior to CT in detecting lymph node metastases and PET scans are more accurate than CT scans in the detection of distant metastases [21–25].

All 12 Asian experts accepted completely ‘recommendations 3d and 3e’ once they had been reworded and combined into a new revised ‘recommendation 3d’ [A = 100%]. The revision was due to the fact that the ESPEN guidelines [26] recommended in the ESMO 2016 oesophageal cancer guidelines [8] are not universally used in Asia, but the importance of malnutrition and weight loss was fully recognised by the representatives of all six oncological societies. The use of the prognostic nutrition index has been validated for oesophageal cancer in both the curative and palliative settings in several Japanese studies [27–31] and the impact of nutritional status and history of weight loss on treatment outcomes following oesophagectomy [32] and chemotherapy [33] demonstrated in trials in Japanese and Chinese patients, respectively. The benefit of nutritional support has not been fully evaluated for palliative chemotherapy in Asian patients but the benefit of nutritional intervention, including enteral nutrition has been demonstrated for Asian patients with oesophageal cancer in the neoadjuvant [34–36] and perioperative settings [37] and reversal of weight loss during chemotherapy has been shown to be associated with an improvement in survival [33].

### Recommendation 4: management of advanced disease

1. **4a. Patients with metastatic oesophageal cancer can be considered for different options of palliative treatment depending on the clinical situation. Single dose brachytherapy may be preferred option even after external RT, since it provides better**
Chemotherapy is indicated for palliative treatment in selected patients, particularly for patients with adenocarcinoma who have a good performance status \( [A = 100\% \text{ and IIIB}] \).

2. **4b. Tumour response to chemotherapy may be predicted early in clinical practice for fit patients \( [A = 100\%] \).**

3. **4c. In squamous cell oesophageal cancer, the value of palliative combination chemotherapy is less proved.** Therefore, best supportive care (BSC) or palliative monotherapy should also be considered. 

All 12 Asian experts accepted the ‘recommendation 4a’ above once it had been revised. Palliative oesophageal cancer treatment aims at preventing or relieving symptoms instead of trying to cure the cancer. The main purpose of this type of treatment is to improve the patient’s comfort and quality of life. External radiotherapy or metal stent placement are usual options for palliative treatment in Asia \( [38] \). Brachytherapy based on the Homs study \( [39] \) and a secondary publication \( [40] \) which for palliative treatment in Asia \( [38] \). Brachytherapy based on the Homs study \( [39] \) and a secondary publication \( [40] \) on which the wording of the ESMO ‘recommendation 4a’ was based, is rarely used in Asia, except in China \( [41] \). However, the usefulness of intraluminal brachytherapy has been investigated in Japan and shown to improve clinical outcome over external radiotherapy alone \( [42, 43] \).

Gastrostomy has been investigated in Asian patients as part of a nutritional palliation approach with encouraging results \( [44] \).

All 12 experts accepted the ‘recommendation 4b’ \( [A = 100\%] \) and ‘recommendation 4c’ once the text had been revised. Palliative chemotherapy is used routinely in Asia in patients with oesophageal adenocarcinoma who have a good performance status. As stated previously in the ESMO 2016 guidelines \( [8] \), there is a paucity of specific evidence relating to the treatment of patients with oesophageal SCC. In Asia, patients with adenocarcinomas of either the distal oesophagus or GEJ are treated the same as patients with metastatic gastric cancer as described previously \( [8] \), and more recently according to the Pan-Asian adapted ESMO guidelines for the treatment of gastric cancer \( [9] \). This means that typically patients with metastatic oesophageal adenocarcinoma will receive first-line doublet platinum fluoropyrimidine therapy. Alternatively, a triplet platinum, fluoropyrimidine, taxane combination regimen may be an option for very fit patients in selected situations such as when a rapid response is desirable due to bulky or symptomatic disease. However, a recent Japanese study has demonstrated no difference in overall survival for patients treated with triplet versus doublet chemotherapy \( [45] \). HER2-positive metastatic oesophageal adenocarcinoma should be treated with a trastuzumab-containing treatment \( [II, B] \) as shown in the ToGA trial \( [12] \).

**Recommendation 5: personalised medicine**

1. **5a. HER2-positive metastatic adenocarcinoma should be treated with a trastuzumab-containing treatment, as was revised as follows:** Trastuzumab-containing treatment is recommended for HER2-positive GEJ adenocarcinomas. It is an option for patients with HER2-negative pure oesophageal adenocarcinomas despite their rarity \( [A = 100\% \text{ and } I, A] \).

2. **5b. Tumour response to chemotherapy may be predicted early by \( ^{18} \text{F-FDG-PET} \) in patients with oesophageal and GEJ adenocarcinomas.** This recommendation was to be deleted.

The Asian experts accepted ‘recommendation 5a’ completely \( [A = 100\%] \) and reworded the ESMO recommendation to be more precise but without changing the meaning. Consistent with ‘recommendation 1’ above, and based on the data from the ToGA trial \( [12, 13, 55] \), and several Asian trials \( [56–61] \). Thus, for patients with HER2-positive oesophageal cancer the recommendations of the Pan-Asian guidelines for mGC \( [9] \) should be followed. ‘Recommendation 5b’ above was recommended to be deleted because it was considered only to be applicable to earlier stage tumours.

The evidence for the role of other novel agents and biomarkers in oesophageal cancer is limited \( [62] \). A randomised phase III UK trial indicated improved progression-free survival with the EGFR tyrosine kinase inhibitor gefitinib, compared with placebo, in patients with advanced oesophageal cancers \( [63] \). Also, EGFR FISH may identify patients who may benefit from gefitinib as second-line treatment \( [64] \). These results, however, need to be confirmed in a prospective study.

Immunohistochemistry for PD-L1 may be a biomarker for pembrolizumab and nivolumab, monoclonal antibodies that bind to the PD-1 receptor. Pembrolizumab has shown promising activity and manageable safety in patients with previously-treated gastric or GEJ cancer, in a global, single-arm phase II trial (KEYNOTE-059) \( [65] \). However, in a phase III study of pembrolizumab versus paclitaxel in patients with advanced cancer of the GEJ (or GC) (KEYNOTE-061) \( [66] \), pembrolizumab therapy was associated with a higher, but statistically non-significant, long-term survival rate compared with paclitaxel in the second-line setting for patients with advanced adenocarcinoma of the GEJ (or GC) and is not recommended for use in this treatment setting.

Nivolumab in a randomised placebo-controlled, phase III trial (ATTRACTION-02) \( [67] \), in Asian patients with advanced GEJ cancer or gastric cancer, pre-treated with at least two lines of chemotherapy and BSC may also be considered in patients with poor performance status. A meta-analysis has shown single-agent irinotecan and taxane therapy to increase survival compared with BSC as second-line therapy \( [53] \).

A limited number of small phase II studies are investigating the role of new agents and have shown hints of activity. For example, a phase II non-randomised trial, of pembrolizumab, an anti-programmed death 1 antibody (anti-PD-1), has demonstrated manageable toxicity and durable antitumor activity in patients with heavily pre-treated, programmed death-ligand 1 (PD-L1)-positive advanced oesophageal carcinoma of both adenocarcinoma and squamous histologies \( [54] \), and studies are ongoing.
prior systemic therapy, showed a statistically significant benefit in overall survival ($P < 0.0001$) compared with placebo regardless of PD-L1 positivity. Studies with different checkpoint inhibitors as monotherapy, or in combination with cytotoxic agents in pre-treated or early lines, and even in the adjuvant setting, are ongoing. Hopefully, the results of these trials will help to inform and focus the relevance of these agents to our future treatment approaches for patients with metastatic oesophageal cancer.

### Discussion

### Conclusions

The results of the voting by the Asian experts both before and after the face-to-face meeting in Kobe showed high concordance (supplementary Tables S1 and S2, available at *Annals of Oncology* online) with the ESMO recommendations for the treatment of patients with metastatic oesophageal cancer published as part of the 2016 'ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up' for oesophageal cancer [8]. In terms of level of agreement there were no votes of less than an A (accept completely) following the face-to-face discussions. Thus, these guidelines can be considered to be consensus guidelines for the treatment of patients with metastatic oesophageal cancer in Asia, with all of the experts (100%) voting to accept completely [A = 100%] each of the recommendations following discussion and some revision in the wording at the face-to-face meeting. Fifty percent of the final recommendations involved some rewording of the original ESMO guidelines [8], mainly due to progress in the field in terms of treatment options. Also, >90% of Asian patients with metastatic oesophageal cancer have SCCs and there are very few trials in these patients. As mentioned previously, the levels of agreement provided by each of the Asian experts were based on the available ‘scientific’ evidence and were independent of the approval and reimbursement status of certain drugs (including biologics) in their individual countries. A summary of the approval and reimbursement status of some of the recommended drugs, as of July 2018, is presented for each participating country in Table 3 and will obviously impact on some of the treatment strategies that can be adopted by certain countries.

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