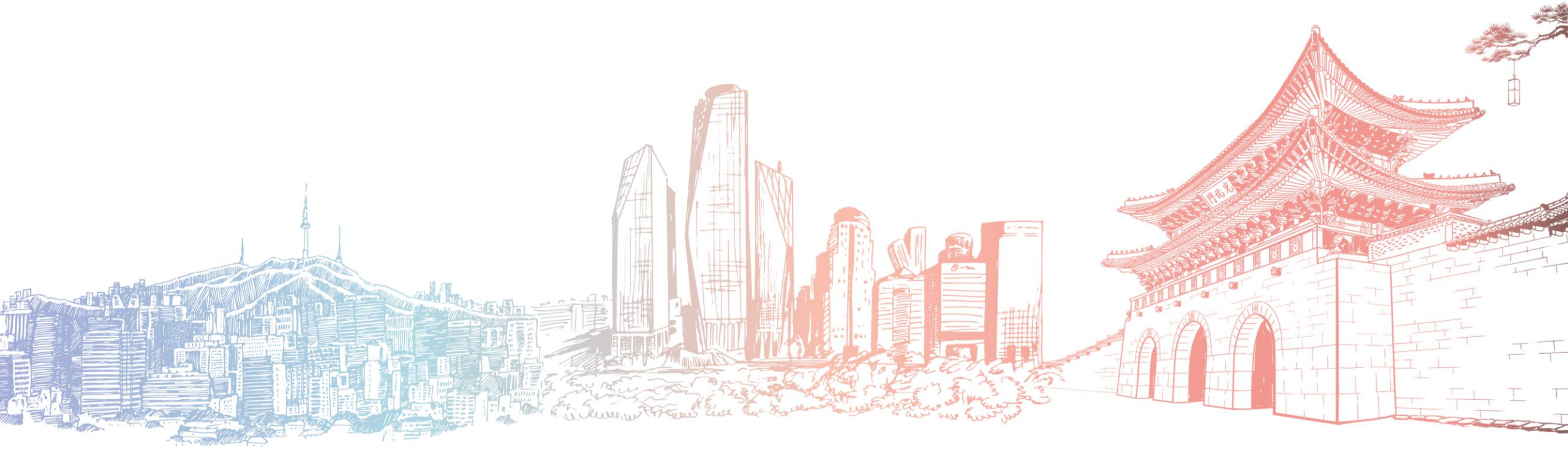
Foundations of the EC management landscape

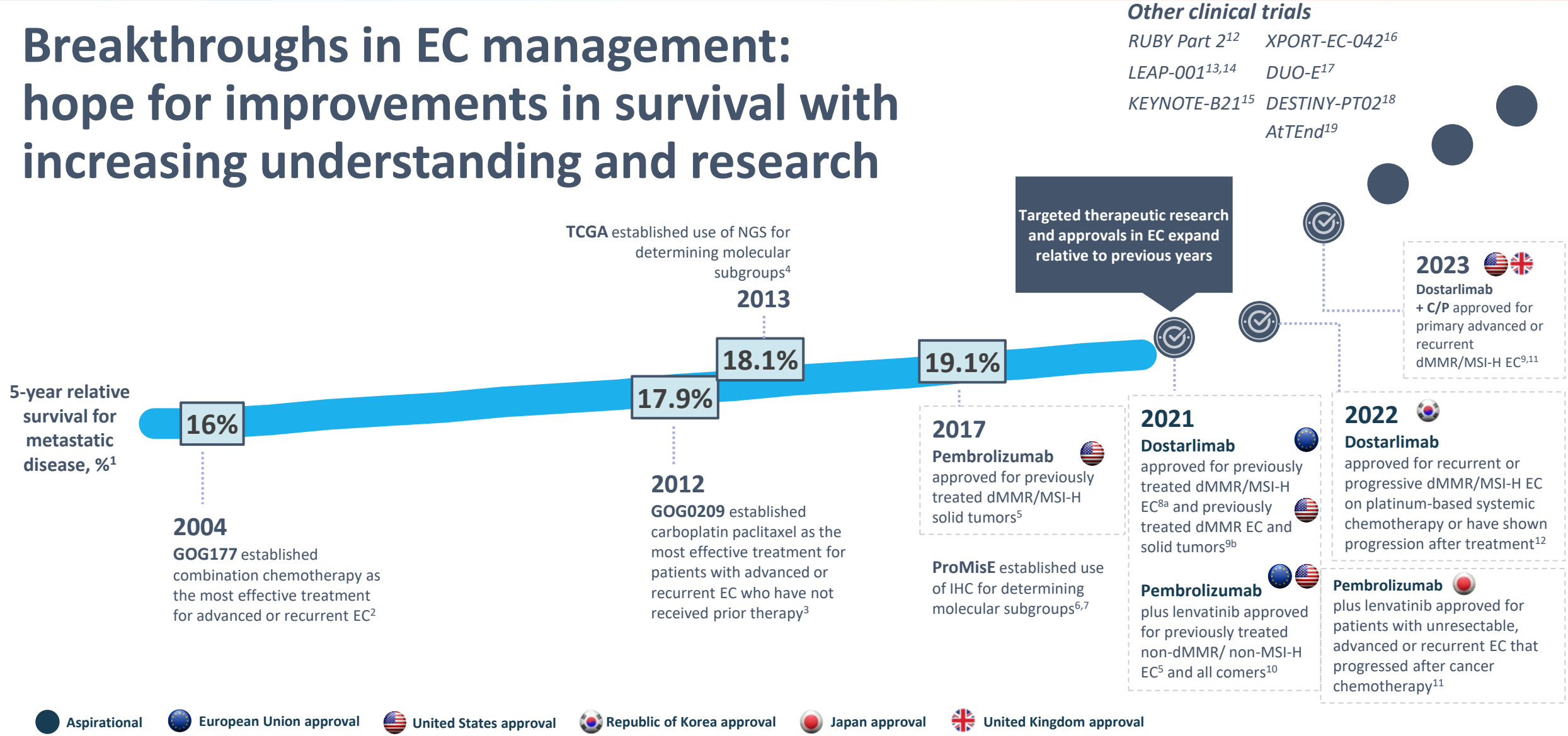
Dr. Byoung-Gie Kim



Disclosures

- Dr. Kim has received research funds from AstraZeneca, MSD, Cellid, and Eutilex
- He has participated in advisory boards for AstraZeneca, MSD, GSK, Takeda, Roche, Cellid, Eutilex, and Gencelmed

Breakthroughs in EC management: hope for improvements in survival with increasing understanding and research



[a]In the EU, dostarlimab is indicated as monotherapy for the treatment of adult patients with dMMR/MSI-H recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen. [b]In the US, dostarlimab is indicated for the treatment of adult patients with dMMR recurrent or advanced endometrial cancer, determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen in any setting and are not candidates for curative surgery or radiation.

C/P = carboplatin/paclitaxel; dMMR = mismatch repair deficient; EC = endometrial cancer; FDA = Food and Drug Administration; GOG = Gynecologic Oncology Group; IHC = immunohistochemistry; MSI-H = microsatellite instability-high; NGS = next generation sequencing; PT = pan-tumor; TGCA = The Cancer Genome Atlas; US = United States.

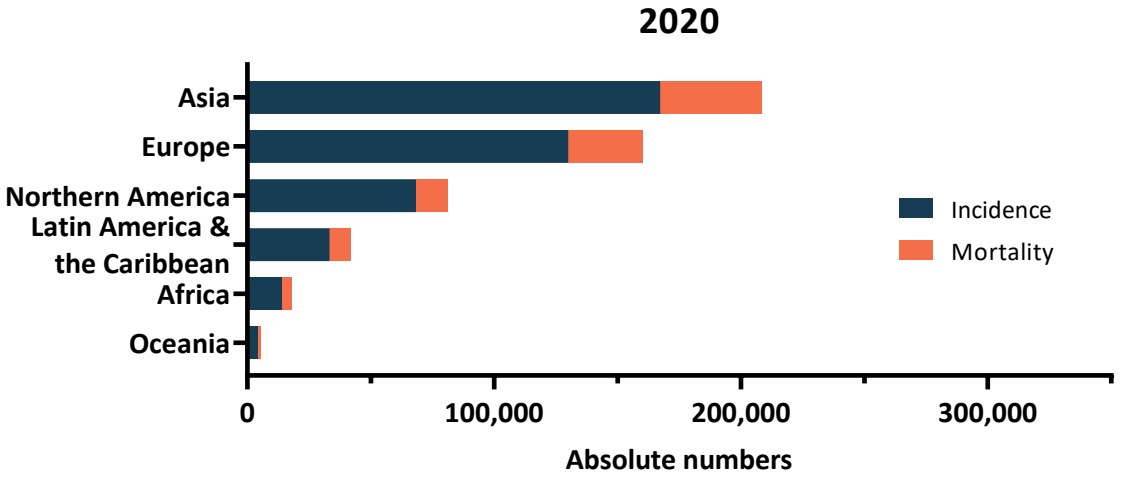
1. National Cancer Institute. SEER Program. Cancer Stat Facts: Uterine Cancer. Available at: https://seer.cancer.gov/statfacts/html/corp.html. Accessed: August 7, 2023. 2. Fleming GF, et al. *J Clin Oncol* 2004. 22:2159-2166. 3. Miller DS, et al. *Gynecol Oncol*. 2012;125:771. 4. Cancer Genome Atlas Research Network et al. Nature 2013;497:67-73. 5. Keytruda (pembrolizumab) [prescribing information]. Merck & Co., Inc., Whitehouse Station, NJ, USA; 2023. 6. Talhouk A et al. *Cancer* 2017;123:802-813. 7. Ventana MMR RxDx Panel (US FDA Approved). Product Information. Tucson, AZ, USA: Ventana Medical Systems, Inc; 2021. 8. Jemperli (dostarlimab) [summary of product characteristics]. GlaxoSmithKline (Ireland) Ltd., Dublin, Ireland; 2023. 9. Jemperli (dostarlimab-gxly) [prescribing information]. GlaxoSmithKline LLC. Philadelphia, PA: 2023. 10. Keytruda (pembrolizumab) [summary of product characteristics]. Merck Sharp & Dohme B.V., Haarlam, The Netherlands; 2022. 11. Jemperli (dostarlimab) [summary of product characteristics]. GlaxoSmithKline UK Limited. Brentford, Middlesex, UK; 2023. 12. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03981796. Accessed on October 13, 2023. 13. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03884101 . Accessed on October 2, 2023. 14. Marth C, et al. *Int J Gynecol Cancer*. 2022;32:92-100. 15. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT04634877. Accessed on October 2, 2023. 16. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT05611931. Accessed on October 2, 2023. 17. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT04269200. Accessed on October 2, 2023. 18. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT04482309. Accessed on October 13, 2023.19. National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT03603184. Accessed on October 2, 2023.

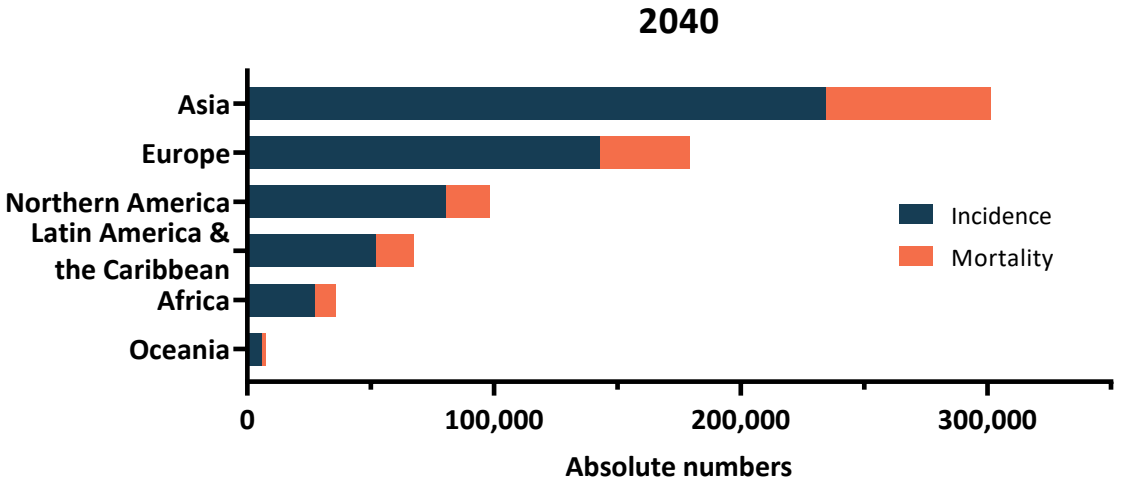
The incidence and mortality of EC continue to rise[1]

EC is the **6th most common** cancer in women worldwide[2]

417,367 new EC cases were recorded globally in 2020; **~40%** of these occurred in **Asia**[3]

EC **mortality** in Asia will increase by **>60%** in coming years[3]

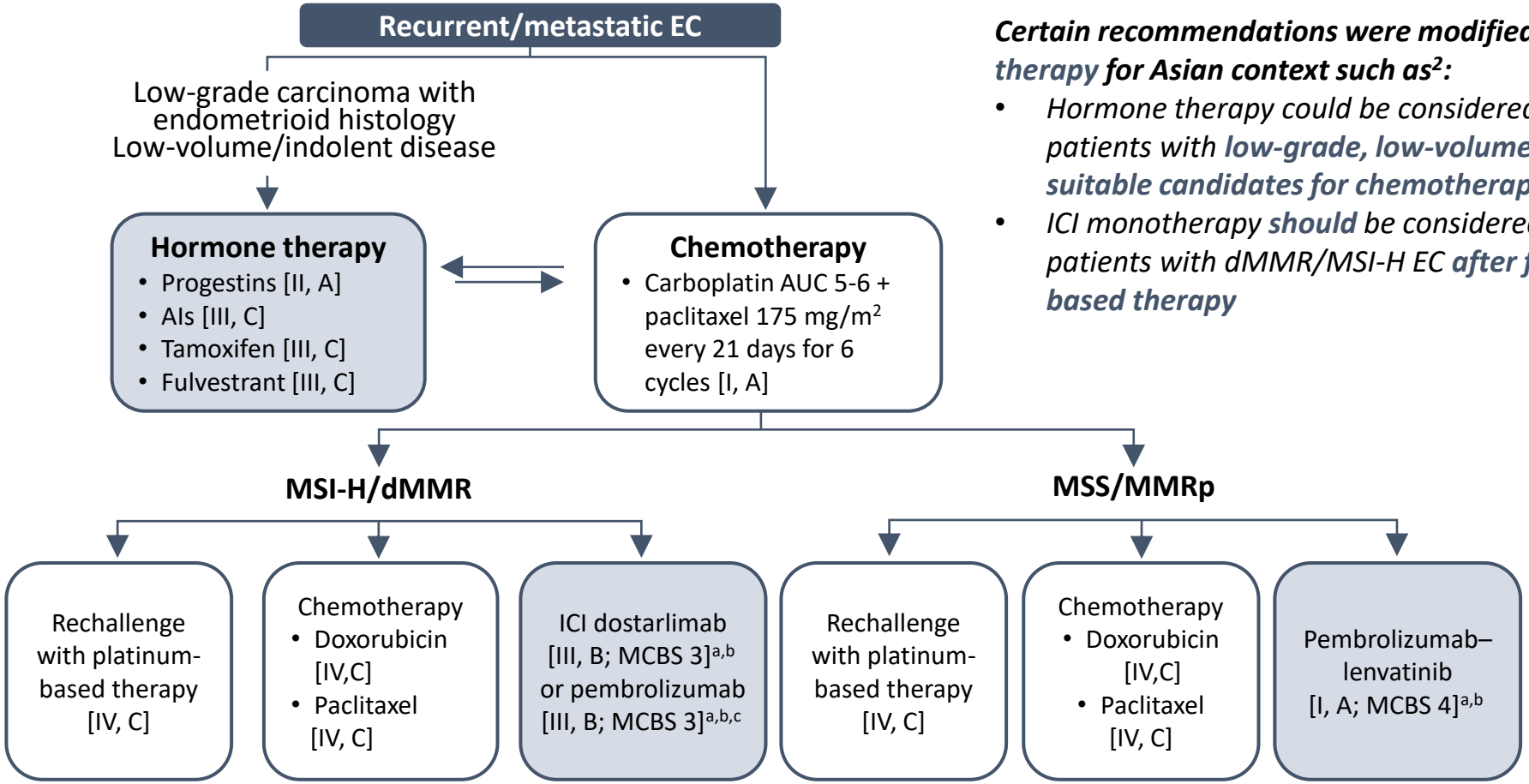




CRS = conditional response rate; EC = endometrial cancer.

1. Cancer Facts & Figures 2023. American Cancer Society. Available at https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf. Accessed January 31, 2023. 2. Sung H, et al. *CA Cancer J Clin*. 2021;71:209-249. 3. International Agency for Research on Cancer. 2023. Available at: https://gco.iarc.fr/tomorrow/ Accessed: August 14, 2023.

Pan-Asian adapted ESMO guidelines for recurrent/metastatic EC[1,2]



Certain recommendations were modified for hormone and ICI therapy for Asian context such as[2]:

- *Hormone therapy could be considered as an 1L option in patients with **low-grade, low-volume disease** who are **not suitable candidates for chemotherapy***
- *ICI monotherapy **should** be considered as an option in patients with dMMR/MSI-H EC **after failure of platinum-based therapy***

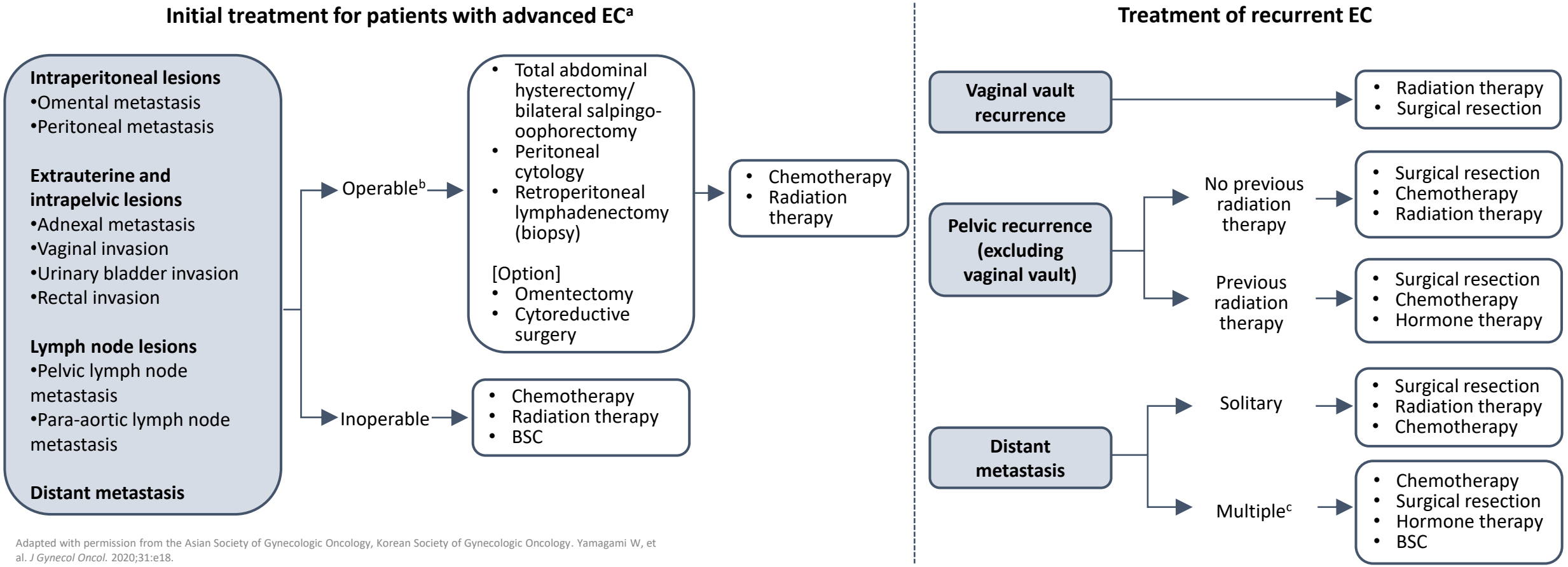
Adapted with permission from the European Society for Medical Oncology.
Oaknin A, et al. *Ann Oncol* 2022;33:860-877.

[a]In patients eligible for further treatment after failure of platinum-based therapy. [b]ESMO-MCBS v1.1 was used to calculate scores for new therapies/indications approved by the European Medicines Agency or Food and Drug Administration (FDA). The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee. [c]FDA approval is restricted to patients whose tumors are not MSI-H or dMMR.

1L = first-line; AI = aromatase inhibitor; AUC = area under the curve; dMMR = mismatch repair deficient; EC = endometrial cancer; ESMO = European Society for Medical Oncology; FDA = Food and Drug Administration; ICI = immune checkpoint inhibitor; MCBS = ESMO-Magnitude of Clinical Benefit Scale; MMRp = mismatch repair proficient; MSI-H = microsatellite instability-high; MSS = microsatellite stable; R/M = recurrent/metastatic.

1. Oaknin A, et al. *Ann Oncol* 2022;33:860-877. 2. Koppikar S, et al. *ESMO Open* 2023;8:100774.

JSGO 2018 guidelines | Chemotherapy is the main treatment for unresectable advanced/recurrent EC, and ICI are yet to be included



Adapted with permission from the Asian Society of Gynecologic Oncology, Korean Society of Gynecologic Oncology. Yamagami W, et al. *J Gynecol Oncol.* 2020;31:e18.

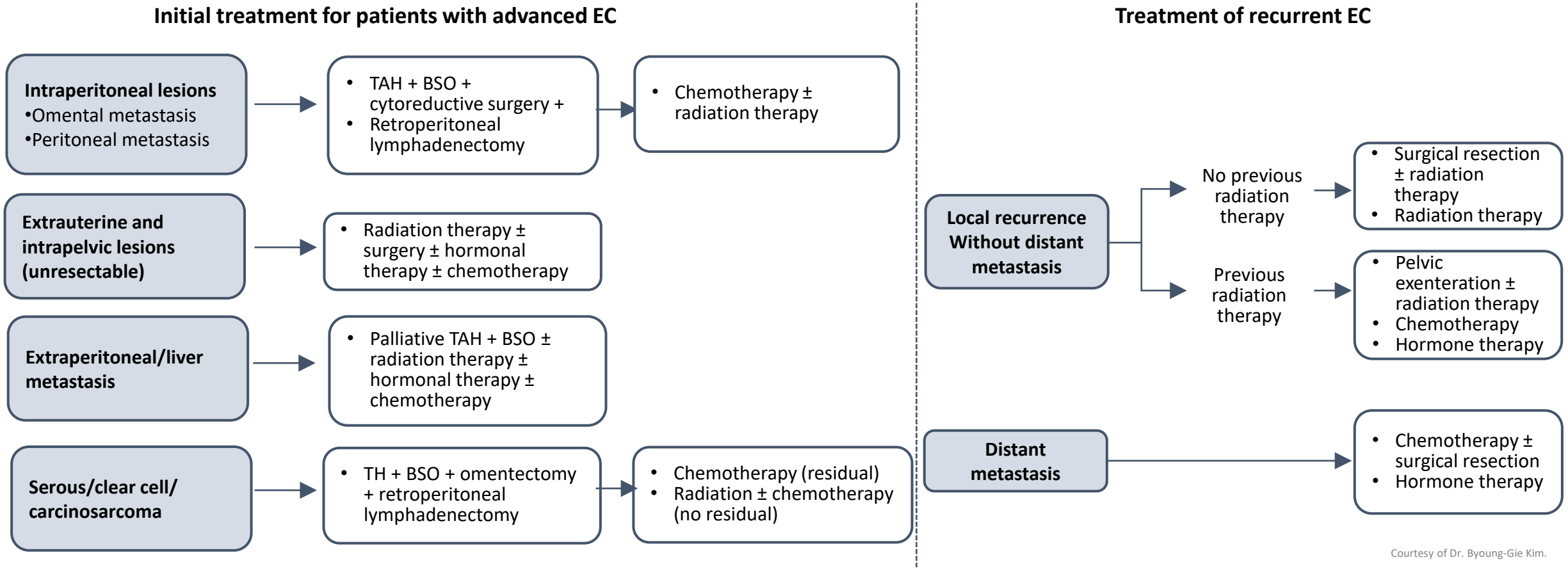
[a]EC considered to be stage III or IV preoperatively. [b]If the general condition is not worse; this refers to all patients in stage III and patients who can undergo hysterectomy and cytoreductive surgery in stage IV. [c]Resection should also be considered for cases with a few small lung metastases.

BSC = best supportive care; EC = endometrial cancer; ICI = immune checkpoint inhibitor; JSGO = Japan Society of Gynegologic Oncolgoy.

Yamagami W, et al. *J Gynecol Oncol.* 2020;31:e18.

KSGO 2020 guidelines | Chemotherapy is the main treatment for unresectable advanced/recurrent EC and ICI are yet to be included[1]

ICI has been approved and prescribed for EC in many Asia-Pacific countries, including Korea[2]

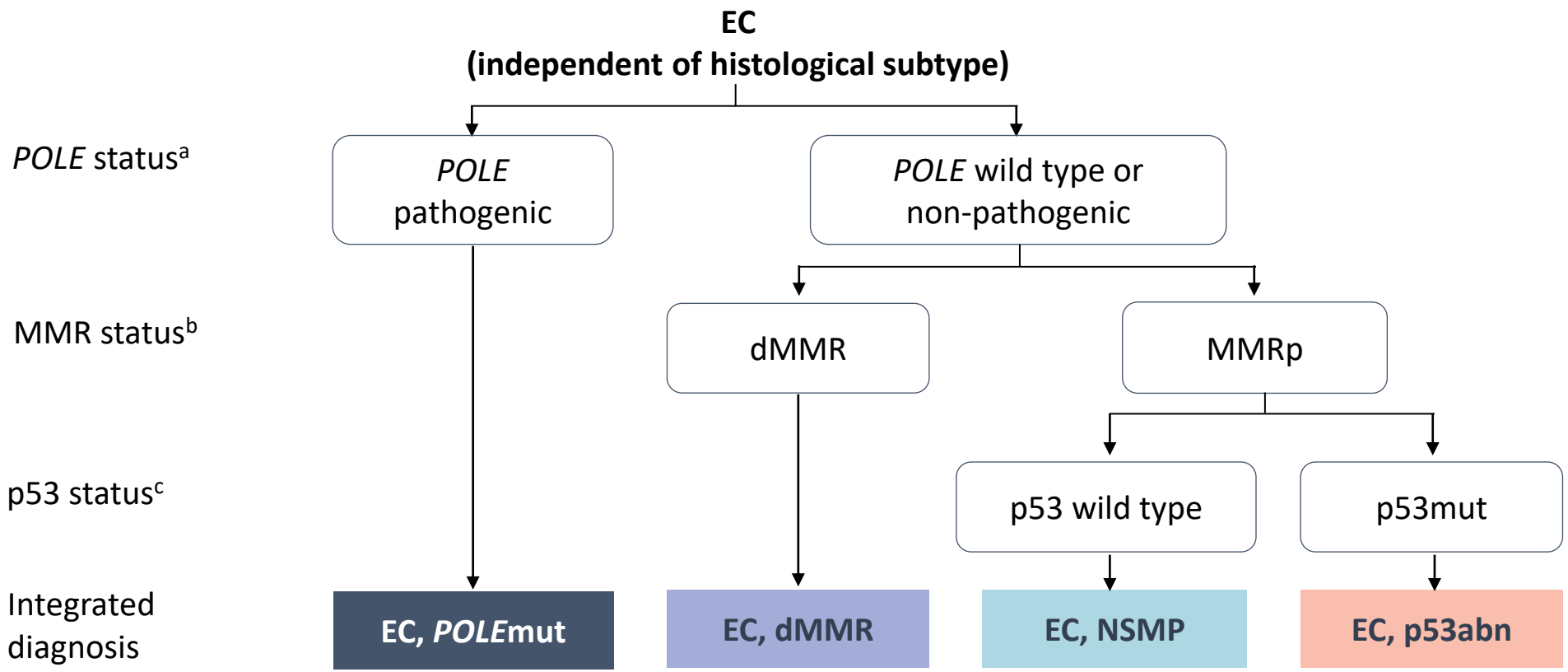


Courtesy of Dr. Byoung-Gie Kim.

BSO = bilateral salpingo oophorectomy; EC = endometrial cancer; ICI + immune checkpoint inhibitor; KSGO = Korean Society for Gynecologic Oncology; TAH = total abdominal hysterectomy; TH = total hysterectomy.

1. Korean Society for Gynecologic Oncology. Guideline for endometrial cancer: available in https://www.sgo.or.kr, 2023 (Korean language). 2. Korea Biomedical Review. Immunotherapy Jemperli mounts 1st reimbursement hurdle half-year after nod. https://www.koreabiomed.com/news/articleView.html?idxno=21342. Accessed October 16, 2023.

Pan-Asian guidelines | Accepted the ESMO diagnostic algorithm for integrated molecular classification of EC[1-3]



Adapted from Vermij L, et al. *Histopathology* 2020;76:52-63.

[a]Pathogenic *POLE* variants include p.Pro286Arg, p.Val411Leu, p.Ser297Phe, p.Ala456Pro, and p.Ser459Phe.25. [b]MMR deficiency is defined by the loss of one or more MMR proteins (*MLH1, PMS2, MSH2, and MSH6*). [c]p53 immunohistochemistry is an acceptable surrogate marker for *TP53* mutation status in MMR-proficient, *POLE* wild-type EC.

dMMR = mismatch repair deficient; EC = endometrial cancer; ESMO = European Society for Medical Oncology; *MLH1* = mutL homolog 1; MMR = mismatch repair; MMRp = mismatch repair proficient; *MSH2/6* = mutS homolog 2/6; NOS = not otherwise specified; NSMP = nonspecific molecular profile; p53 = tumor suppressor protein 53; p53mut = tumor suppressor protein 53 mutated; p53abn = p53 abnormal; *PMS2* = PMS1 homolog 2; *POLE* = polymerase-ε; *POLEmut* = polymerase ε-mutated; *tp53* = tumor suppressor protein 53.

1. Koppikar S, et al. *ESMO Open.* 2023;8:100774. 2. Oaknin A, et al. *Ann Oncol* 2022;33:860-877. 3. Vermij L, et al. *Histopathology* 2020;76:52-63.