2021 ESMO congress

1758O
Neoadjuvant pembrolizumab in localized/locally advanced solid tumors with mismatch repair deficiency

K. Ludford[1], K. Raghav[1], M.A. Blum Murphy[1], N.D. Fleming[2], D. Nelson[1], M.S. Lee[1], B.G. Smaglo[1], Y.N. You[3], M.M. Tillman[4], C. Kamiya-Matsuoka[5], S. Thirumurthi[6], C. Messick[4], B. Johnson[1], E. Vilar[7], J. Thomas[1], W.C. Foo[8], W. Qiao[9], S. Kopetz[1], M.J. Overman[1]

[1] Gastrointestinal Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA, [2] Gynecologic Oncology and Reproductive Medicine, MD Anderson Cancer Center, Houston, TX, USA, [3] Colon and Rectal Surgery, MD Anderson Cancer Center, Houston, TX, USA, [4] Surgical Oncology, MD Anderson Cancer Center, Houston, TX, USA, [5] Neuro-Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [6] Gastroenterology, Hepatology and Nutrition, MD Anderson Cancer Center, Houston, TX, USA, [7] Clinical Cancer Prevention, MD Anderson Cancer Center, Houston, TX, USA, [8] Pathology, Anatomical, MD Anderson Cancer Center, Houston, TX, USA[9] Biostatistics, MD Anderson Cancer Center, Houston, TX, USA

Background

Pembrolizumab (pembro) significantly improves clinical outcomes in advanced/metastatic microsatellite instability high (MSI-H)/deficient mismatch repair (dMMR) solid tumors. This study evaluates pembro in the neoadjuvant space with the potential for an organ-sparing approach.

Methods

This is a phase 2 open-label, single center trial of MSI-H/dMMR non-metastatic solid tumors with localized unresectable or high risk resectable (defined as ≥ 20% recurrence) with measurable disease. Treatment is Pembro 200mg every 3 wks for 8 cycles followed by surgical resection with option to continue therapy for 18 cycles followed by observation. First restaging is at 6 wks and includes baseline and 3-week 70-gene ctDNA assessment. To continue on study, patients are required to have PR/CR, SD with tumor shrinkage or SD with decline in ctDNA. The co-primary endpoints are safety and pathological complete response (pCR). Key secondary endpoints are response rate and organ-sparing at one year for patients who declined surgery.

Results

Between 10/2019 and 3/2021, 35 pts were enrolled and study has completed enrollment. Tumor types included 27 CRC and 8 non-CRC: endometrial, gastric, meningioma, 2 duodenal, ampullary and 2 pancreatic. Median follow-up was 9 months (range 0.1 - 17). Among 32 evaluable pts, best ORR was 75% (CR 25% , PR 50%), SD 22% and PD 3%. Luminal endoscopic response was seen in 17/19 (89%) pts. Among 8 (23%) pts who underwent surgery, pCR was seen in 4. At present non-operative approach was chosen by 8 (23%) pts with 1-year organ-sparing seen in 2/2 evaluable pts. Treatment-related grade 3/4 immune adverse events were seen in 3 (9%) pts (transaminitis, diarrhea and type 1 diabetes). Baseline ctDNA mutations were present in 20 (57%) pts and at 3 weeks declined in 15 (75%), unchanged in 1, no paired 3 week sample in 1, and increased in 3. Tumor microenvironment immune analysis is ongoing and will be presented.

Conclusions

Neoadjuvant pembrolizumab in dMMR/MSI-H cancers is safe and resulted in high rates of radiographic and endoscopic response which has implications for organ-sparing strategies. Non-operative management of dMMR/MSI-H localized solid tumors should be further investigated.

Clinical trial identification

NCT04082572.

Legal entity responsible for the study

The authors.

Funding

Merck.

Disclosure

All authors have declared no conflicts of interest.