Tumor Board Tuesday – Dr. Joao Fogacci, 4/26/2022: A Rare But Great Opportunity in Gastric Cancer

Posttest Rationale

1. Which are potentially useful immunotherapy biomarkers in gastric cancer?
    A. CPS PDL1
    B. MMRd/MSI-H
    C. TMB-H
    D. All above

Rationale: Option A: Despite FDA (and also Brazilian agency) approval for ICB+Chemo regardless of CPS PDL1 based on the CM649 trial, we can see that the best survival benefit occurs in CPS =/> 5. And other meta-analyses (CM649 and KN062) also showed less benefit from ICB in CPS 1-4.

Option B: This is an agnostic test to predict the benefit of immunotherapy that we can use for many tumors.

Option C: This is also FDA agnostic approval with cutoff =/> 10 mut/MB based on KN158 trial. This is also listed in the NCCN guideline as a biomarker.

References: Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. *Lancet*. 2021;398(10294):27-40. doi:10.1016/S0140-6736(21)00797-2

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Wang F, Wei XL, Wang FH, et al. Safety, efficacy and tumor mutational burden as a biomarker of overall survival benefit in chemo-refractory gastric cancer treated with toripalimab, a PD-1 antibody in phase Ib/II clinical trial NCT02915432. *Ann Oncol*. 2019;30(9):1479-1486. doi:10.1093/annonc/mdz197

2. What is special about MUTYH mt biallelic tumors?
    A. TMB, PDL1 & KRAS G12C
    B. Causes only CRC/polyposis
    C. HER2 amplification
    D. <50% develop CRC

Rationale: MUTYH mutated tumors are varied, and they have potential for immunotherapy.

References: Nieuwenhuis MH, Vogt S, Jones N, et al. Evidence for accelerated colorectal adenoma--carcinoma progression in MUTYH-associated polyposis?. *Gut*. 2012;61(5):734-738. doi:10.1136/gut.2010.229104

Win AK, Reece JC, Dowty JG, et al. Risk of extracolonic cancers for people with biallelic and monoallelic mutations in MUTYH [published correction appears in Int J Cancer. 2017 Dec 15;141(12):E7]. *Int J Cancer*. 2016;139(7):1557-1563. doi:10.1002/ijc.30197

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