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Metastatic mismatch repair deficiency cancers: Hard to find, but delight to treat!

Amit Rauthan, Nitin Yashas, Poonam Patil, Rajashri, Pratyush, Chinnu, S.P. Somashekhar, Shabber Zaveri
Comprehensive Cancer Center, Manipal Hospital, Bangalore, India
amitrauthan@yahoo.com

ManipalHospitals
LIFE'S ON

BACKGROUND

- Metastatic cancers with mismatch repair (MMR) deficiency are rare and seen in about 5% of metastatic cancer patients.
- Most commonly seen in cancers of the uterus and gastrointestinal tract.
- They show very good and durable response to treatment with immunotherapy (PD1 blockade), leading to a tumor agnostic approval in this indication.
- Limited data of MMR deficient patients treated with immunotherapy from India.

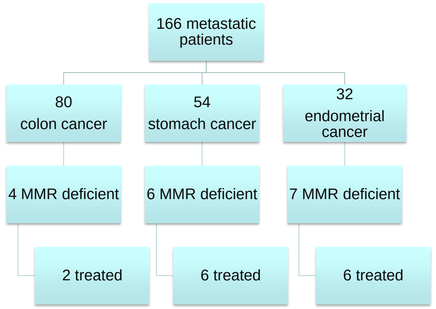
OBJECTIVE

- This is a single center, retrospective study of patients with metastatic mismatch repair (MMR) deficiency cancers who received immunotherapy.
- The endpoints were objective response rate (ORR), progression free survival (PFS) and overall survival (OS).

METHODS

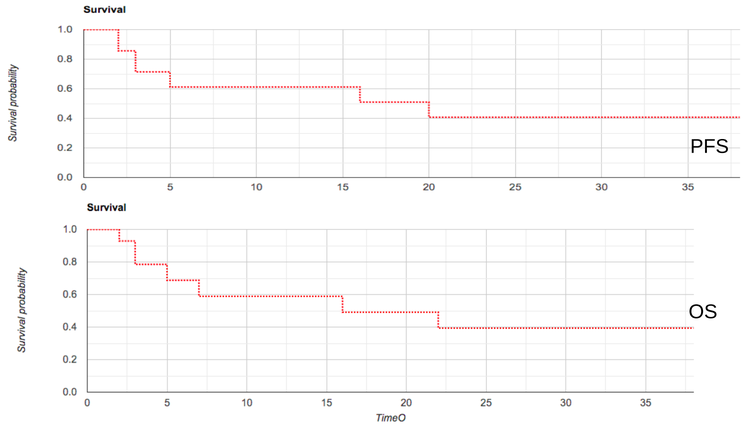
- Between Jan 2018 to Jan 2021, 166 metastatic cancer patients were tested for MMR deficiency by immunohistochemistry
- Primary site: colon in 80, stomach in 54, uterus in 32 patients
- Of these: 4,6,7 patients respectively had MMR deficiency (17 patients = 10.2%)
- Fourteen MMR deficient patients who had progressed on at least one line of chemotherapy received immunotherapy with either nivolumab or pembrolizumab
- Primary site - stomach: 6, uterus: 6 and colon: 2 patients
- Males: 7 and females: 7
- Median age was 58 years (37-81 years)
- Immunotherapy as second line = 7, third line = 6 and fourth line = 1 patient.

PATIENT CHARACTERISTICS

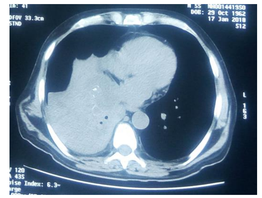


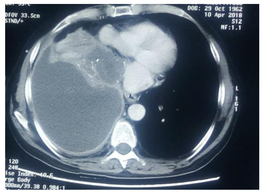
RESULTS

- The number of cycles ranged from 2 to 50
- The ORR was 64.3%
  - Partial Response (PR) 9 (64.3%)
  - Stable Disease 1 (7.1%)
  - Progressive disease 4 (28.6%)
- Median PFS was 18 months (2-38 months)
- Median OS was 22 months
- 4 patients have crossed 2 years without progression, and 2 patients have crossed 3 years without progression



RESULTS





Patient with MMR deficient carcinoma colon with lung metastases, completed 30 cycles of nivolumab and has completed > 3 years without progression

Jan 2018- pre nivolumab

April 2018- after 6 doses of nivolumab

CONCLUSION

- MMR deficient metastatic cancers are uncommon and are seen in 10% of patients in our study.
- MMR testing by immunohistochemistry is an easy, quick and cost effective test for picking up this population.
- Immunotherapy with nivolumab or pembrolizumab showed a high ORR and durable response in our patients, inspite of being given in second line and beyond setting.
- Recent first line immunotherapy data is practice changing and will need evaluation in our deficient MMR patients.
- It is imperative that we check every metastatic cancer for MMR deficiency, as this patient population; even though rare, has the potential to become long term survivors.
- MMR testing also helps us identify patients for further germline testing to screen for Lynch syndrome.

REFERENCES

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DISCLOSURES

- Dr Amit Rauthan discloses Consulting or Advisory Role - AstraZeneca; Bristol-Myers Squibb; Cipla; Eisai; Lilly; Merck; MSD; Novartis; Pfizer; Roche India.