The clinical utility and safety of Immune check point inhibitors (ICI) - Multicentric data from India

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Background

Immunotherapy has emerged as a new treatment option cancer care in last one decade and is the standard of care in many difficult to treat cancers. The real world data of immunotherapeutic agents from Low and middle income countries (LMICs) like India is scarce due to under representation in multinational clinical trials, lack of accessibility and high cost [1]Pharmacogenomic variations with varied practices can potentially affect efficacy and safety and merits exploration.

Aim

To study the safety and efficacy of ICI in an Indian multicenter setting

Objectives

To enumerate the overall survival (OS) and progression free survival (PFS) of ICI used in India for solid tumors.

To study the prevalence of toxicities and tolerance of ICI in Indian population

Methods

This is a retrospective multi-centric observational study on the safety and efficacy of ICIs in adult solid tumors between August 2014 to March 2019 from 14 centers in India. Data on the pattern of care, PFS, OS , toxicities were obtained for various indications in India. Final data was analyzed using SPSS software version 22. Survival analysis was plotted using Kaplan Meier Curves

Results

There were 750 patients with median age of 59(16-85) years with male preponderance (75.8%). The most common indications for ICI were Non small cell lung carcinoma (NSCLC) 276 (41.6%) followed by HNSCC n=132 (20%).Nearly half of the patients received ICI as second line (n=322, 49.2%). ICI were given first line in 79 (12.1%) mostly for NSCLC and melanoma. The median duration of therapy is 2.5(0.5-21) months. The median number of cycles of ICI received was 4 (1-41). Complete or partial responses were seen in 107 (21%) and stable disease noted in 125 (24.6%) (Response rate =45.6%) [table 1]. Pseudoprogression was confirmed in 7 cases, 1%. The most common toxicities observed were anemia 9.5% (n=63) and fatigue 5.4% (n=36) [table 2]. The occurrence of grade 3 and 4 toxicities like pneumonitis, colitis, nephritis and thyroiditis were <1% and were managed as per standard guidelines. There was no toxicity related mortalities reported. The median OS with the use of ICI in solid tumors is 16 (12- 29) months [Fig .1] and PFS is 4(3-5) months [Fig 2]. The median OS and PFS for each cancer are highlighted in table 3.

Conclusion

Despite short term ICI use, real world multicentric data from India confirms the clinical benefit of ICI in in various solid tumors and is comparable to international literature. The tolerance is acceptable and there were no additional safety signals observed in this population. Short course therapy should be further explored in larger cohort in randomised fashion for reproducibility.

Table 1 showing the response rates in patients with solid tumors

Response	No (N)	Percentage
Complete response (CR)	20	3.9
Partial response (PR)	87	17.1
Stable disease (SD)	125	24.6
Progressive disease (PD)	136	26.7
Not evaluated	137	26.9
Pseudoprogression	6	0.8

Table 2 showing toxicities associated with immune check point inhibitors

Toxicities	Percentage (number)
Anemia	9.5 (63)
Fatigue	5.4 (36)
Thrombocytopenia	0.8 (5)
Neutropenia	2.9 (19)
Thyroiditis/hypothyroidism	2.1 (17)
Myalgia	1.3 (8)
Rash/skin reactions	1.5 (10)
Pneumonitis	1.0 (7)
Colitis	0.7 (5)
Nephritis	0.9(6)

Table 3 showing the median OS and PFS in each cancer from the date of start of immune check point inhibitors

Type of malignancy	Median OS in months (95% upper and lower confidence interval)	Median PFS in months (95% upper and lower confidence interval)
NSCLC	15 (11-NA)	4 (3-5)
Renal cell carcinoma RCC	20 (8-NA)	5 (3-9)
HNSCC	Not reached	7 months (4-10)
Melanoma	Not reached	4 months (3-NA)
Hepatocellular carcinoma	6months (1-14)	1 month (1-12)
Gastrointestinal (esophagus, stomach, colorectal)	8 (4-NA)	3 (2-7)
Urothelial carcinoma	Not reached	3 Months (2-NA)

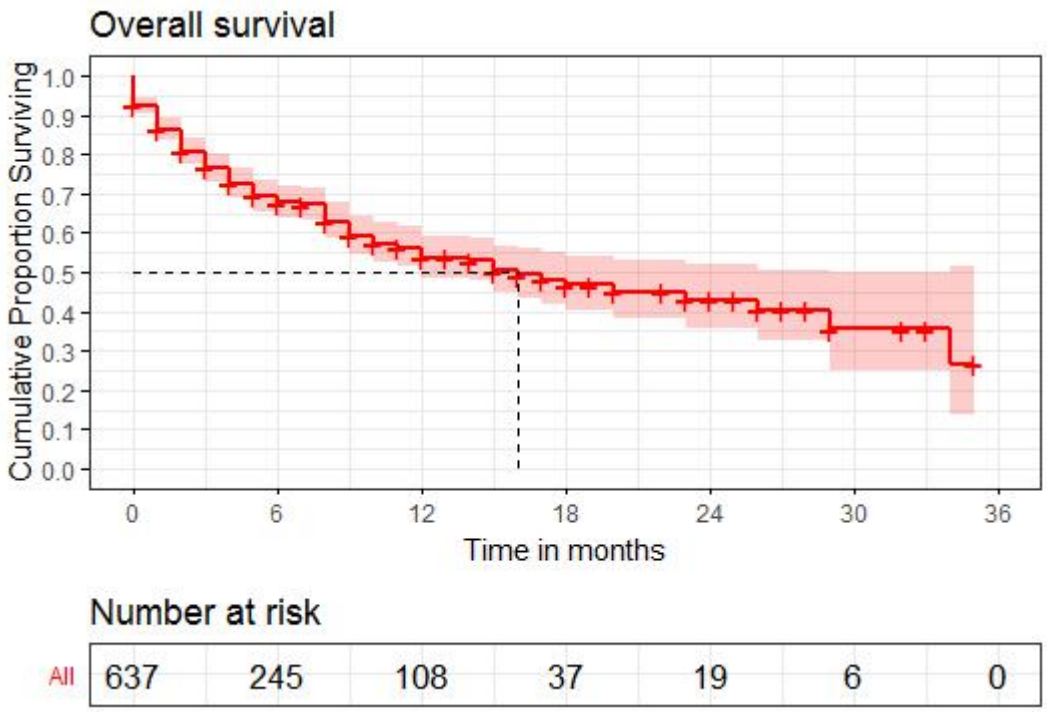

Fig.1 Kaplan Meier plot demonstrating the overall survival with immune check point inhibitors in solid tumors

Fig 2 Kaplan Meier plot demonstrating the progression free survival with immune check point inhibitors in solid tumors.

Bibliography

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