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Immune-mediated adverse events (imAEs) associated with sasanlimab in combination with Bacillus Calmette-Guérin (BCG): Phase III study (CREST)

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Background

Sasanlimab in combination with BCG induction and maintenance (I+M) significantly prolonged event-free survival vs BCG-I+M for patients (pts) with BCG-naive, high-risk NMIBC, with an acceptable safety profile in the phase 3 CREST study. Here, we report the incidence and management of imAEs from CREST.

Methods

Eligible pts were randomized 1:1:1 to receive sasanlimab with BCG-I+M, sasanlimab with BCG-I, or BCG-I+M. AEs were classified as imAEs using programmatic checks and medical review based on the known safety profiles of immune checkpoint inhibitors (ICIs) and were reported using NCI CTCAE v5.0.

Results

At data cutoff (Dec 2, 2024), rates of imAEs were similar between the sasanlimab with BCG-I+M (n=350; any grade: 43%; grade ≥3: 16%) and sasanlimab with BCG-I (n=348; any grade: 47%; grade ≥3: 14%) arms. In the pooled data from the sasanlimab with BCG-I+M and sasanlimab with BCG-I arms (Table), any-grade imAEs occurred in 45% of pts (312/698); most pts with an imAE had grade 1/2 as the highest grade (67%; 208/312). The most common any-grade imAEs by clusters were thyroid disorders (19%) and rash (13%). The most common grade ≥3 imAEs by cluster were hepatitis and rash (3% each). The most common imAEs leading to discontinuation of sasanlimab were rash and hepatitis (3% each). Systemic corticosteroids were administered in 139 of 312 pts (45%) who had an imAE, 77 of whom had received a high dose (≥40 mg daily prednisolone or equivalent). Hormonal replacement therapy was required for 74% of pts with an immune-mediated thyroid disorder. All pts with immune-mediated Type 1 diabetes required insulin. At the data cutoff, 40% of pts with an imAE had all imAEs resolved. Table: 3078P

Pts, n (%)	Sasanlimab with BCG (pooled) N=698
Any-grade imAE	312 (45)
Grade 1	64 (9)
Grade 2	144 (21)
Grade 3	86 (12)
Grade 4	17 (2)
Grade 5	1 (<1) ^a
imAE clusters	
Thyroid disorders	133 (19)
Rash	94 (13)
Hepatitis	29 (4)
Pancreatitis	24 (3)

Pts, n (%)	Sasanlimab with BCG (pooled) N=698
Adrenal insufficiency	24 (3)
Colitis	18 (3)
Hypophysitis/hypopituitarism	17 (2)
Nephritis and renal dysfunction	15 (2)
Pneumonitis	14 (2)
Type 1 diabetes	11 (2)
Myocarditis	4 (<1)
Myositis	3 (<1)
Myasthenic syndrome/myasthenia gravis	2 (<1)
Uveitis	1 (<1)
Other imAEs	24 (3)
Pts with imAEs leading to sasanlimab discontinuation	112 (16)
Pts with imAEs leading to BCG discontinuation	11 (2)
Pts with all imAEs resolved ^b	125 (40)

^aMyocarditis. ^bOf pts with an imAE (n=312).

Conclusions

imAEs seen with sasanlimab in combination with BCG were aligned with the known safety profile of ICIs. imAEs were manageable with treatment interruption/discontinuation and administration of corticosteroids and/or hormonal replacement therapy.

Clinical trial identification

NCT04165317.

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Legal entity responsible for the study

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Disclosure

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