

Background

- Dostarlimab is a humanized programmed death 1 (PD-1) receptor monoclonal antibody that blocks interaction with the ligands PD-L1 and PD-L2



In the EU, dostarlimab is approved as a monotherapy in adult patients with recurrent or advanced mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) endometrial cancer (EC) that has progressed on or after treatment with a platinum-containing regimen¹



In the US, dostarlimab is approved as a monotherapy in adult patients with the following:

- dMMR recurrent or advanced EC that has progressed on or after a platinum-containing regimen²
- a dMMR solid tumor that has progressed on or after prior treatment and who have no satisfactory alternative treatment options³
- GARNET (NCT02715284) is a phase 1 study assessing the antitumor activity and safety of dostarlimab monotherapy in patients with solid tumors⁴

Conclusions

- Safety with dostarlimab was consistent with the anti-PD-1 drug class
- Safety was consistent across tumor types
- Most treatment-related adverse events (TRAEs) were low grade, with few leading to interruption or discontinuation
- No overall increase in the rate of TRAEs was seen after transitioning to the 1000-mg Q6W dosing schedule

Poster #991-P

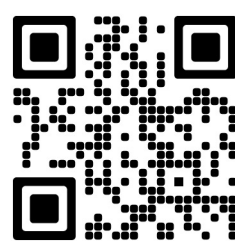


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Presented at the European Society for Medical Oncology (ESMO) 2021 Congress, 16–21 September 2021.

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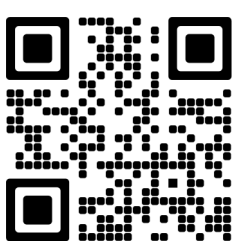
Acknowledgments

- This study (NCT02715284) was funded by GlaxoSmithKline (Waltham, MA).
- Writing and editorial support, funded by GlaxoSmithKline (Waltham, MA, USA) and coordinated by Heather Ostendorf-Bach, PhD, of GlaxoSmithKline, were provided by Shannon Morgan-Pekol, PhD, and Jennifer Robertson, PhD, of Ashfield MedComms, an Ashfield Health company (Middletown, CT, USA).

Conflicts of Interest

Dr. André has served in a consulting/advisory role and/or received honoraria from Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Chugai, Clovis, GlaxoSmithKline, Gritstone Oncology, Halodex, Kaleido Biosciences, MSD Oncology, Pierre Fabre, Roche/Ventana, Sanofi, and Servier, and has received travel, accommodation, and expenses from Bristol-Myers Squibb, MSD Oncology, and Roche/Genentech.

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Treatment-Related Adverse Events Occurring During Dostarlimab Therapy in the GARNET Study

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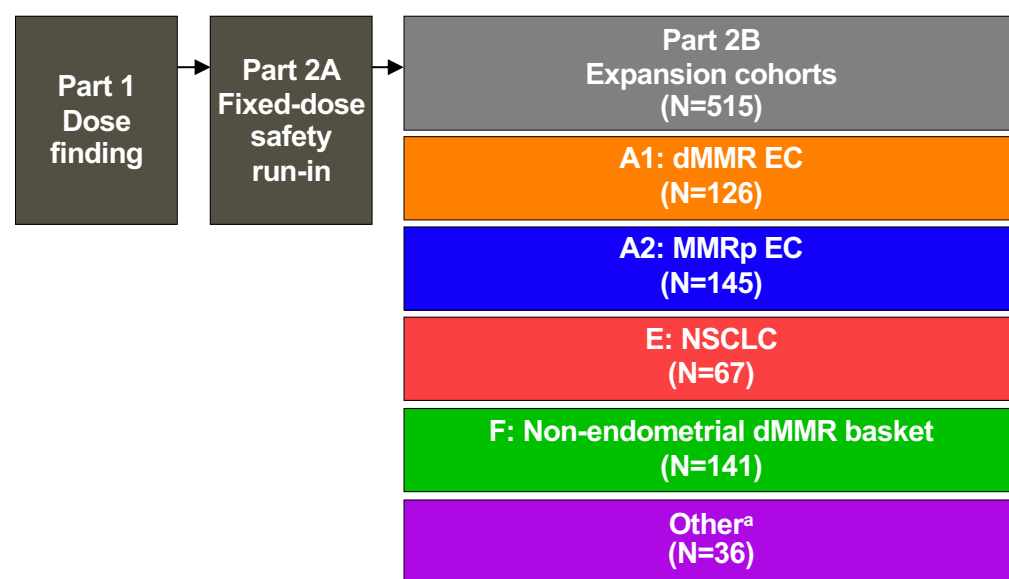
Objective

- To report on TRAEs and immune-related TRAEs (irTRAEs) across the part 2B expansion cohorts of the GARNET trial

Methods

- This multicenter, open-label, single-arm study is being conducted in 2 parts: dose escalation and expansion (Figure 1)
- In part 2B, dostarlimab was administered at the recommended therapeutic dose determined from parts 1 and 2A (Figure 2)

Figure 1. GARNET Trial Design



*Other includes 19 patients with MMR status unknown EC, 13 patients with MMR status unknown non-EC, 4 patients with MMRp non-EC, dMMR, mismatch repair deficient; EC, endometrial cancer; MMR, mismatch repair; MMRp, mismatch repair proficient; MSI-H, microsatellite instability high; NSCLC, non-small cell lung cancer.

Figure 2. GARNET Study Dosing Schedule

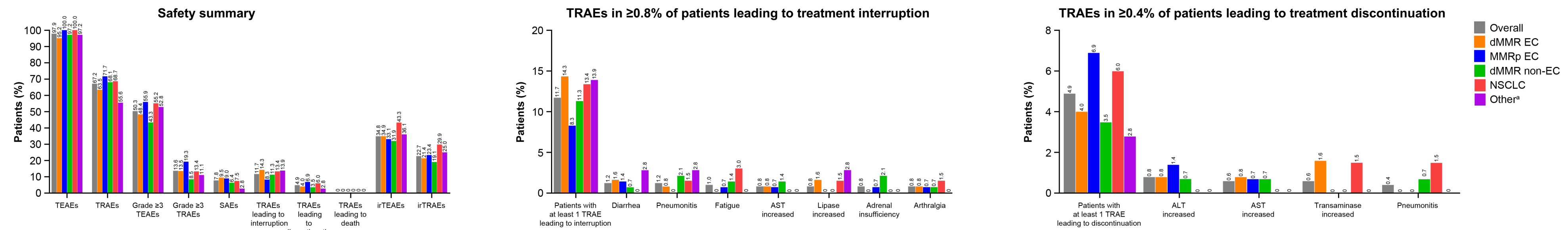
500 mg Q3W (1 cycle = 3 weeks)				1000 mg Q6W until disease progression or unacceptable toxicity (1 cycle = 6 weeks)			
Cycle	1	2	3	4	5	6	7
Week	1	4	7	10	13	19	25

Q3W, every 3 weeks; Q6W, every 6 weeks.

- MMR status was determined by immunohistochemistry
- Primary endpoints were objective response rate and duration of response
- Data cutoff date was March 1, 2020

Results

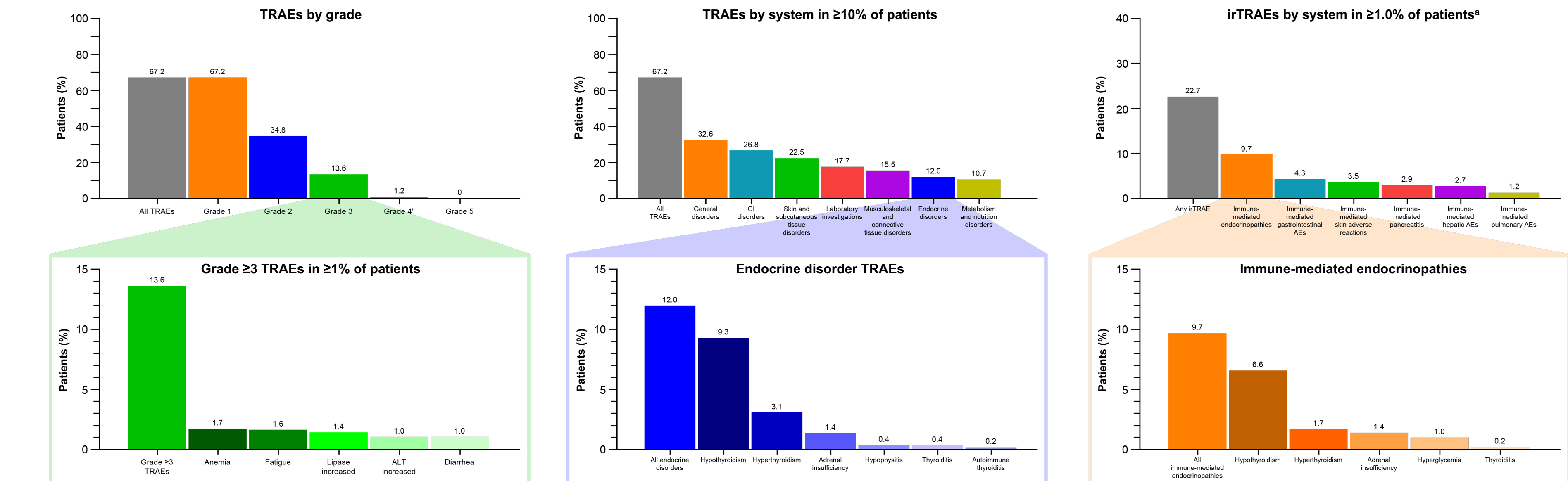
Figure 3. Safety Events Across Cohorts



*Other includes 19 patients with MMR status unknown EC, 13 patients with MMR status unknown non-EC, and 4 patients with MMRp non-EC.

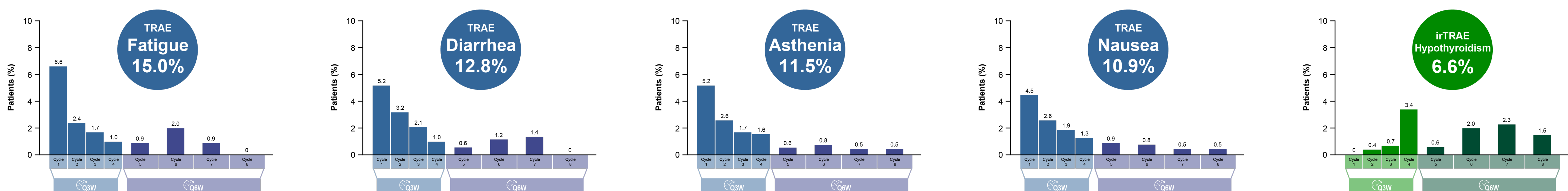
ALT, alanine aminotransferase; AST, aspartate aminotransferase; dMMR, mismatch repair deficient; EC, endometrial cancer; ir, immune-related; MMR, mismatch repair; MMRp, mismatch repair proficient; NSCLC, non-small cell lung cancer; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Figure 4. TRAEs and irTRAEs by System and Grade



*Immune-related AEs are defined as irTRAEs grade ≥2; †Grade 4 TRAEs were lipase increased (0.4%), amylase increased (0.2%), aspartate aminotransferase increased (0.2%), autoimmune hemolytic anemia (0.2%), gamma-glutamyltransferase increased (0.2%), and hyperlipasemia (0.2%). AE, adverse event; ALT, alanine aminotransferase; GI, gastrointestinal; ir, immune-related; TRAE, treatment-related adverse event.

Figure 5. Time Course of TRAEs in ≥10% of Patients and irTRAEs in ≥5% of Patients



ir, immune-related; Q3W, every 3 weeks; Q6W, every 6 weeks; TRAE, treatment-related adverse event.

Safety events were consistent across tumor types

- 97.9% experienced a TEAE
- 67.2% experienced a TRAE
- 11.7% experienced TRAEs leading to interruption
- 4.9% experienced TRAEs leading to discontinuation

The majority of TRAEs and irTRAEs were low grade

- 13.6% experienced a grade ≥3 TRAE
- 7.2% experienced a grade ≥3 irTRAE

TRAEs were spread across all systems

- Few patients experienced endocrine-disorder TRAEs (12.0%) or immune-mediated endocrinopathies (9.7%)

No spike in the rate of TRAEs or irTRAEs was seen at dose change from 500 mg IV Q3W to 1000 mg IV Q6W