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

Thierry André,[1] Dominique Berton,[2] Ana Oaknin,[3] Victor Moreno,[4] Giuseppe Curigliano,[5] José Trigo,[6] Maria-Pilar Barretina-Ginesta,[7] Susan Ellard,[8] Anna V. Tinker,[9] Rowan Miller,[10] Joanna Pikiel,[11] Valentina Boni,[12] Sara Cresta,[13] Bhavana Pothuri,[14] Desamparados Roda,[15] Yvette Drew,[16] Jennifer Veneris,[17] Ellie Im,[17] Susan Banerjee[18]*

[1]Sorbonne University and Saint-Antoine Hospital, Paris, France; [2]GINECO & Institut de Cancerologie de l'Ouest, Centre René Gaudducheau, Saint-Herblain, France; [3]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [4]START Madrid-FJD, Fundación Jiménez Díaz Hospital, Madrid, Spain; [5]Division of Early Drug Development for Innovative Therapies, IEO, European Institute of Oncology IRCCS, and University of Milano, Milan, Italy; [6]Medical Oncology Department, Hospital Universitario Virgen de la Victoria, Málaga, Spain; [7]Institut Català d'Oncologia, Girona, Spain; [8]BC Cancer–Kelowna, British Columbia, Canada; [9]BC Cancer, Vancouver, British Columbia, Canada; [10]University College London, St. Bartholomew's Hospital London, London, UK; [11]Regional Center of Oncology, Gdansk, Poland; [12]START Madrid CIOCC (Centro Integral Oncológico Clara Campal), Hospital Universitario HM Sanchinarro, Madrid, Spain; [13]IRCCS Istituto Nazionale dei Tumori Foundation, Milan, Italy; [14]Gynecologic Oncology Group (GOG) and Department of Obstetrics/Gynecology, Laura & Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [15]Department of Medical Oncology, University Hospital, Valencia, Spain; [16]Northern Centre for Cancer Care, Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; [17]GlaxoSmithKline, Waltham, MA, USA; [18]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK.*

[*]Employed by GlaxoSmithKline when the study was conducted.

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 regimen[1]

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 regimen[2]
- a dMMR solid tumor that has progressed on or after prior treatment and who have no satisfactory alternative treatment options[3]

- GARNET (NCT02715284) is a phase 1 study assessing the antitumor activity and safety of dostarlimab monotherapy in patients with solid tumors[4]

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

Presenting author email:
thierry.andre@aphp.fr

Scan to download a copy of this poster

Scan to download data tables

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

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

[a]Other includes 19 patients with MMR status unknown EC, 13 patients with MMR status unknown non-EC, and 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

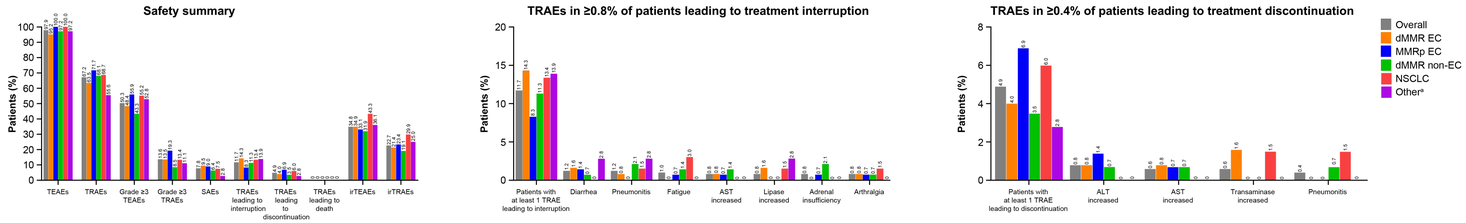
	500 mg Q3W (1 cycle = 3 weeks)				1000 mg Q6W until disease progression or unacceptable toxicity (1 cycle = 6 weeks)			
Cycle	1	2	3	4	5	6	7	Continue dosing Q6W
Week	1	4	7	10	13	19	25	

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

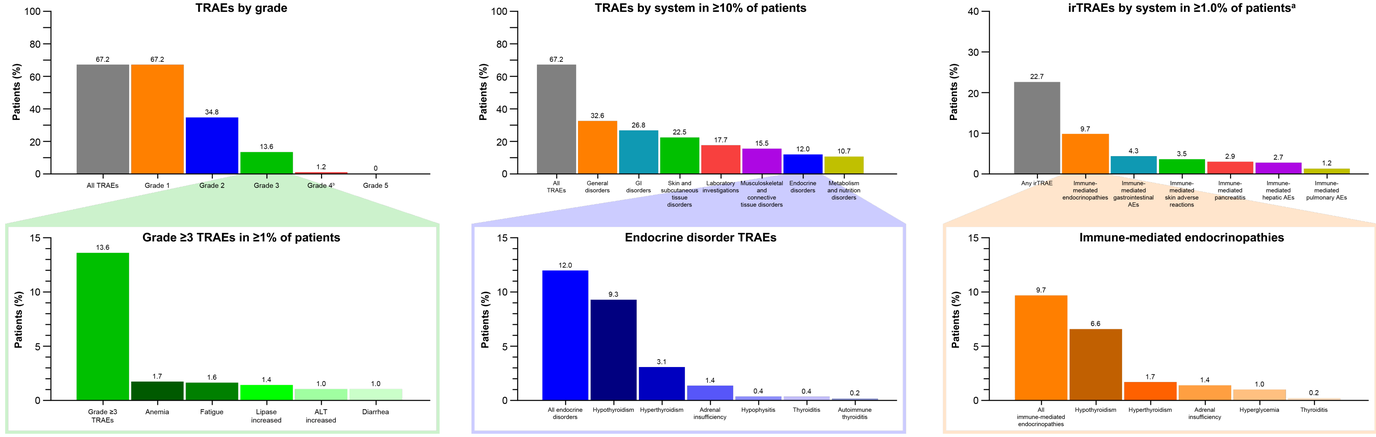


[a]Other includes 19 patients with MMR status unknown EC, 13 patients with MMR status unknown non-EC, and 4 patients with MMRp non-EC.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; dMMR, mismatch repair deficient; EC, endometrial cancer; ir, immune-related; MMR, mismatch repair; MMRp, mismatch repair proficient; NSCLC, non–small cell lung cancer; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

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

Figure 4. TRAEs and irTRAEs by System and Grade



[a]Immune-related AEs are defined as irTRAEs grade ≥2; [b]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.

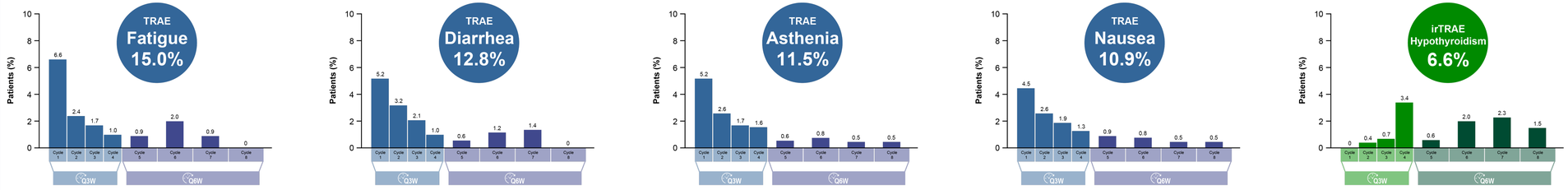
The majority of TRAEs and irTRAEs were low grade

- 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%)

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.

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

References

1. European Medicines Agency. Jemperli. https://www.ema.europa.eu/en/medicines/human/EPAR/jemperli. Accessed May 24, 2020.
2. GlaxoSmithKline. Jemperli. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761174s000lbl.pdf. Accessed August 23, 2021.
3. US Food and Drug Administration. FDA grants accelerated approval to dostarlimab-gxly for dMMR advanced solid tumors. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dostarlimab-gxly-dmmr-advanced-solid-tumors. Accessed August 23, 2021.
4. ClinicalTrials.gov. Study of TSR-042, an anti-programmed cell death-1 receptor (PD-1) monoclonal antibody, in participants with advanced solid tumors (GARNET): NCT02715284. https://clinicaltrials.gov/ct2/show/NCT02715284. Accessed May 6, 2021.

Acknowledgments

This study (NCT02715284) was funded by GlaxoSmithKline (Waltham, MA)
Writing and editorial support, funded by GlaxoSmithKline (Waltham, MA, USA) and coordinated by Heather Ostendorff-Bach, PhD, of GlaxoSmithKline, were provided by Shannon Morgan-Pelosi, 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, Halioδx, 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.

Scan to download full author conflicts of interest