BERLIN 2025 ESMO congress

LBA92

3-weekly docetaxel 75 mg/m2 vs 2-weekly docetaxel 50 mg/m2 in combination with darolutamide + ADT in patients with mHSPC: Results from the randomised phase III ARASAFE trial

M-O. Grimm[1], G. Von Amsberg[2], H. Heers[3], S. Degener[4], F. Roghmann[5], J. Casuscelli[6], S. Rausch[7], M. Augustin[8], L. Häberle[9], K. Leucht[1], A. Roessler[1], F. Zengerling[10]

[1] Department of Urology, Jena University Hospital, Jena, Germany, [2] Department of Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [3] Department of Urology, Philipps University Marburg, Marburg, Germany, [4] Department of Urology, Helios University Hospital Wuppertal, Wuppertal, Germany, [5] Department of Urology, Marien Hospital Herne, Herne, Germany, [6] Department of Urology, Ludwig-Maximilians University, Munich, Germany, [7] Department of Urology, Tubingen University Hospital, Tuebingen, Germany, [8] Department of Hematology and Oncology, Nuremberg Hospital, Campus Nord, Nürnberg, Germany, [9] BioMed Statistics GmbH, Erlangen, Germany[10] Department of Urology, Ulm University Hospital, Ulm, Germany

Background

Triple therapy with androgen deprivation therapy (ADT), darolutamide (daro), and docetaxel (doce) is approved for metastatic hormone-sensitive prostate cancer (mHSPC). The pivotal ARASENS trial (NCT02799602) used doce 75 mg/m^2 Q3W. Daro triple therapy with doce 50 mg/m^2 Q2W is hypothesized to reduce grade 3-5 adverse events (AEs) vs 75 mg/m^2 Q3W.

Methods

In this academic, randomised, open-label, multicentre phase 3 trial (NCT05676203), 250 men with mHSPC were randomised 1:1 (JUN 2023 – DEC 2024) to receive ADT, daro, and 6 cycles of doce 75 mg/m^2 Q3W (3-week cycle; D75) or 50 mg/m^2 Q2W (4-week cycle; D50). Primary objective was to compare grade 3-5 AE rates 26 weeks after last patient first doce dose (LPFD) in the safety population, followed by the rate of grade 3/4 neutropenia or death from any cause (NAER) as secondary safety variable.

Results

In the safety population, 128 patients received doce in the D75 arm and 121 in the D50 arm. Patient populations were well balanced between the two treatment arms (Table). Mean cumulative docetaxel doses were 842.8 mg for D75 (standard deviation ±181.7 mg) and 1073.5 mg (±240.4 mg) for D50, respectively. The study met its primary endpoints, demonstrating a significantly lower incidence of grade 3-5 AEs for D50 (D50: 61.2% [95% CI 51.9, 69.9] vs D75: 78.9% [70.8, 85.6]; p=0.0024). Also NAER was significantly reduced for D50 (D50: 24.0% [16.7, 32.6] vs D75: 64.1% [55.1, 72.3]; p<0.00001). At 26 weeks after LPFD, median PSA was 0.26 ng/ml (IQR 0.05, 1.55) and 0.16 ng/ml (0.03, 1.00) for D50 and D75, respectively. The PSA-response rate (PSA≤0.2 ng/ml) was higher in D75 (41.3% vs 48.8%).Table: LBA92

	Docetaxel 75 mg/m^2 Q3W, N=129	Docetaxel 50 mg/m^2 Q2W, N=121
Age, median (IQR), years	68.0 (63.0, 74.0)	67.0 (63.0, 73.0)
Metastases at primary diagnosis, n (%)	102 (79.7)	108 (89.3)
Metastasis pattern at study entry, n (%)		
- Non-regional lymph node only	1 (0.8)	0 (0.0)
- Bone / non-visceral	108 (83.7)	107 (88.4)
- Visceral / other	20 (15.5)	14 (11.6)
High volume disease, n (%)	108 (83.7)	104 (86.0)
Alkaline phosphatase ≥ ULN, n (%)	73 (56.6)	73 (60.3)
Serum PSA, median (IQR), ng/ml	12.2 (2.2, 75)	14.7 (3.6, 57.7)

Conclusions

ARASAFE demonstrates a statistically highly significant and clinically meaningful reduction in the incidence of grade 3-5 AE rate and NAER for the D50 approach, which may be considered a potential new standard of care. Further follow-up is ongoing to determine its efficacy in terms of oncological outcomes.

Clinical trial identification

EU CT:2022-502634-52-00; NCT05676203.

Legal entity responsible for the study

Jena University Hospital, represented by Prof. Dr. Marc-Oliver Grimm.

Funding

Bayer Vital GmbH.

Disclosure

M. Grimm: Financial Interests, Personal, Advisory Board: AstraZeneca, Bayer, Bristol Myers Squibb, Ipsen Pharma, Merck Serono, MSD, Pfizer, Roche, Eisai, Janssen Cilag, Gilead, Novartis, Telix, Astellas, Kranus, Recordati, Roche; Financial Interests, Personal, Invited Speaker: AstraZeneca, Bristol Myers Squibb, Ipsen Pharma, Merck Serono, MSD, Janssen, Astellas, Bayer, Novartis; Financial Interests, Personal and Institutional, Coordinating PI: Bristol Myes Squibb; Financial Interests, Institutional, Local PI: Intuitive Surgical; Financial Interests, Institutional, Coordinating PI: Bayer. H. Heers: Financial Interests, Personal, Other, Invited speaker and writer for a peri-ESMO conference newsletter and podcast project: Ipsen; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Royalties: Springer Healthcare; Financial Interests, Institutional, Local PI: AstraZeneca, BMS, MSD, Merck Serono, Ipsen. J. Casuscelli: Financial Interests, Personal, Invited Speaker: Johnson&Johnson, Pfizer, AstraZeneca, Bristol Myers Squibb, Ipsen, Astellas; Financial Interests, Personal, Advisory Board: MSD, Merck; Non-Financial Interests, Principal Investigator: MSD, AstraZeneca. S. Rausch: Financial Interests, Personal, Advisory Board: Merck Serono, Bayer, Eisai, MSD; Financial Interests, Personal, Invited Speaker: Ipsen, Lilly, Janssen-Cilag, Pfizer, Amgen, AstraZeneca, Merck Serono, Bayer, Astellas; Financial Interests, Personal, Writing Engagement: BMS; Financial Interests, Institutional, Local PI: Merck, Pfizer, Merck Serono, Steba Biotech, Lilly, Roche, AstraZeneca, Aveo Pharmaceuticals, BMS, Eisai, Exelixis, Immunomedics, Bicycle Therapeutics, Ipsen, Janssen-Cilag, Seattle Genetics, Gilead; Financial Interests, Personal, Coordinating PI: TriNetX, LCC. L. Häberle: Financial Interests, Personal, Ownership Interest, I am a shareholder of Biomed Statistics GmbH (limited liability company): BioMed Statistics GmbH. K. Leucht: Financial Interests, Institutional, Writing Engagement: Intuitive Surgical, Bristol Myers Squibb; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Writing Engagement: UroTrials. A. Roessler: Financial Interests, Institutional, Other, Travel expenses: Bayer Vital GmbH; Financial Interests, Personal, Full or part-time Employment, Managing Partner: UroTrials GmbH. F. Zengerling: Financial Interests, Personal, Advisory Board: Apogepha Pharma GmbH, AstraZeneca Germany GmbH, Bristol Myers Squibb GmbH, Roche Pharma GmbH, Daiichi Sankyo; Financial Interests, Personal, Advisory Board, Consulting fees and honoraria for lectures: Astellas Pharma GmbH, Bayer Vital GmbH, Ipsen Pharma GmbH, Janssen-Cilag GmbH, Merck Healthcare Germany GmbH, Pfizer Pharma GmbH, MSD, Novartis; Financial Interests, Personal, Invited Speaker: Amgen. All other authors have declared no conflicts of interest.