2021 ESMO congress

LBA26

Darolutamide maintenance in metastatic castration resistant prostate cancer (mCRPC) previously treated with novel hormonal agents (NHA) and non-progressive disease after subsequent treatment with a taxane: A randomized double-blind placebo-controlled phase II trial (SAKK 08/16)

R. Cathomas[1], G. Procopio[2], S. Hayoz[3], E.A. Kremer[4], D. Kienle[5], O. Caffo[6], D. Lorente[7], A. Pedrazzini[8], G. Roubaud[9], S. Nenan[10], A.G. Omlin[11], C. Buttigliero[12], R.J. Pereira Mestre[13], K. Ribi[4], S. Gillessen[14]

[1] Oncology/Hematology, Kantonsspital Graubünden, Chur, Switzerland, [2] Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, [3] SAKK - Swiss Group for Clinical Cancer Research, Bern, Switzerland, [4] Coordinating Center, SAKK - Swiss Group for Clinical Cancer Research, Bern, Switzerland, [5] Division of Hematology/Oncology, Kantonsspital Graubünden, Chur, Switzerland, [6] Medical Oncology Department, Presidio Ospedaliero Santa Chiara, Trento, Italy, [7] Medical Oncology Department, Consorci Hospitalari Provincial de Castellón, Castellon, Spain, [8] Medical Oncology Department, Fondazione Oncologia Lago Maggiore, Locarno, Switzerland, [9] Medical Oncology, Institute Bergonié, Bordeaux, France, [10] Département de la recherche et développement, Unicancer, Paris, France, [11] Medical Onocolgy and Haematology Department, Kantonsspital St. Gallen, St. Gallen, Switzerland, [12] Department of Oncology, University of Torino at S. Luigi Hospital, Torino, Italy, [13] Oncology Department, EOC - Ospedale Regionale Bellinzona e Valli - Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona, Switzerland[14] Medical Oncology, EOC - Ospedale Regionale Bellinzona e Valli - Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona, Switzerland

Background

Treatment options for patients (pts) with mCRPC have evolved with introduction of NHAs. We hypothesize that maintenance treatment with Darolutamide (Daro) for pts with disease stabilization under chemotherapy after pretreatment with another NHA can delay disease progression.

Methods

SAKK 08/16 is a randomized placebo-controlled double-blind phase 2 study. Pts with mCRPC and prior NHA therapy and non-progressive disease on taxane (docetaxel >=300mg/m^2 or cabazitaxel >=80mg/m^2) were eligible. Pts received Daro 600mg bd or placebo bd starting 2-8 weeks (wks) after end of taxane. Primary endpoint: radiographic progression-free survival at 12 wks (rPFS12). Secondary endpoints: rPFS, event-free survival (EFS), overall survival (OS), PSA 50% response (PSA50 RR), adverse events (AE). 88 pts were needed to show superiority of Daro for rPFS12 (type I error 15%, power 80%).

Results

92 pts were accrued between 3/17 – 11/20. Median follow-up is 18 months (mo). Median age was 72 years (55-87). Prior taxane was docetaxel in 93% and cabazitaxel in 7%. Prior NHA was Abiraterone in 60%, Enzalutamide in 31% and both in 9%. rPFS12 was significantly improved with Daro 64.7% vs placebo 52.2% (p=0.127, below significance level of 0.15). Median rPFS on Daro was 5.5 mo vs 4.5 mo on placebo (HR 0.54; 95% CI 0.32-0.91; p=0.017) and median EFS 5.4 mo vs 2.9 mo (HR 0.46; 95% CI 0.29-0.73; p=0.001). PSA50 RR was 22% on Daro vs 4% on placebo (p=0.014). Median OS on Daro was 24 mo vs 21.3 mo on placebo (HR 0.62; 95% CI 0.3-1.26; p= 0.181). Treatment related AEs were mild and similar in both arms (Daro vs placebo): G1 26% vs 22%, G2 13% vs 15%, G3 2% vs 2%. Fatigue G1/2 was less common in Daro arm (11% vs 20%).

Conclusions

This proof of concept study met its primary endpoint and shows that switch maintenance with Daro after prior taxane and at least one NHA results in a statistically significant but clinically modest prolongation of rPFS and EFS with good tolerability. Median OS with Daro maintenance is promising and numerically superior to the control arm.

Clinical trial identification

NCT02933801.

Legal entity responsible for the study

SAKK Swiss Working Group for Clinical Cancer Research.

Funding

Bayer and SERI (Swiss State Secretariat for Education, Research and Innovation).

Disclosure

R. Cathomas: Financial Interests, Institutional, Advisory Board: AstraZeneca; Financial Interests, Institutional, Advisory Board: BMS; Financial Interests, Institutional, Advisory Board: Bayer; Financial Interests, Institutional, Advisory Board: MSD; Financial Interests, Institutional, Advisory Board: Roche; Financial Interests, Institutional, Advisory Board: Sanofi; Financial Interests, Institutional, Advisory Board: Astellas; Financial Interests, Institutional, Advisory Board: Ipsen; Financial Interests, Institutional, Advisory Board: Merck; Financial Interests, Institutional, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Institutional, Advisory Board: Debiopharm; Financial Interests, Personal, Invited Speaker: Janssen; Financial Interests, Institutional, Invited Speaker: Astellas. G. Procopio: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Institutional, Research Grant: Ipsen; Financial Interests, Institutional, Research Grant: Novartis. O. Caffo: Financial Interests, Personal, Advisory Board: Astellas; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Sanofi; Financial Interests, Personal, Advisory Board: AAA. A.G. Omlin: Financial Interests, Institutional, Advisory Board: AstraZeneca; Financial Interests, Institutional, Advisory Board: Astellas; Financial Interests, Institutional, Advisory Board: Bayer; Financial Interests, Institutional, Advisory Board: Janssen; Financial Interests, Institutional, Advisory Board: Molecular Partners; Financial Interests, Institutional, Advisory Board: MSD; Financial Interests, Institutional, Advisory Board: Pfizer; Financial Interests, Institutional, Advisory Board: Roche; Financial Interests, Institutional, Advisory Board: Sanofi; Financial Interests, Institutional, Research Grant: TEVA; Financial Interests, Institutional, Research Grant: Janssen; Financial Interests, Institutional, Speaker's Bureau: Astellas; Financial Interests, Institutional, Speaker's Bureau: Bayer; Financial Interests, Institutional, Speaker's Bureau: Janssen. S. Gillessen: Financial Interests, Institutional, Other: Janssen; Financial Interests, Institutional, Other: RSI; Financial Interests, Institutional, Advisory Role: AAA; Financial Interests, Institutional, Advisory Role: Amgen; Financial Interests, Institutional, Advisory Role: Aranda; Financial Interests, Institutional, Advisory Role: Astellas; Financial Interests, Institutional, Advisory Role: Bayer; Financial Interests, Institutional, Advisory Role: BMS; Financial Interests, Institutional, Advisory Role: Janssen; Financial Interests, Institutional, Advisory Role: Menarini Silicon Biosystems; Financial Interests, Institutional, Advisory Role: MSD; Financial Interests, Institutional, Advisory Role: MSD; Financial Interests, Institutional, Advisory Role: Orion; Financial Interests, Institutional, Advisory Role: Pfizer; Financial Interests, Institutional, Advisory Role: Roche; Financial Interests, Institutional, Advisory Role: Sanofi; Financial Interests, Institutional, Advisory Role: Telixpharma; Financial Interests, Institutional, Advisory Role: Toledo Pharmaceuticals; Financial Interests, Institutional, Other: Proteomedix. All other authors have declared no conflicts of interest.