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Kim N Chi | kchi@bccancer.bc.ca

Haematologic impact of [^{177}Lu]Lu-PSMA-617 versus ARPI change in patients with metastatic castration-resistant prostate cancer in PSMAfore

Kim N Chi,[1] Oliver Sartor,[2] Karim Fizazi,[3] Johann S de Bono,[4] Neal D Shore,[5] Ken Herrmann,[6] Daniel Castellano,[7] Josep M Piulats,[8] Aude Fléchon,[9] Xiao X Wei,[10] Hyun Kim,[11] Michael T Schweizer,[12] Shaheen Alanee,[13] Samson Ghebremariam,[14] Marianna Hertelendi,[15] Michael J Morris[16]

[1]BC Cancer, Vancouver, BC, Canada; [2]Mayo Clinic, Rochester, MN, USA; [3]Gustave Roussy Institute, Paris-Saclay University, Villejuif, France; [4]The Institute of Cancer Research and The Royal Marsden Hospital, London, UK; [5]Carolina Urologic Research Center and GenesisCare US, Myrtle Beach, SC, USA; [6]University Hospital Essen, Essen, Germany; [7]Hospital Universitario 12 de Octubre, Madrid, Spain; [8]Catalan Institute of Oncology, Barcelona, Spain; [9]Centre Léon Bérard, Lyon, France; [10]Dana-Farber Cancer Institute, Boston, MA, USA; [11]Washington University in St. Louis, St. Louis, MO, USA; [12]University of Washington and Fred Hutchinson Cancer Center, Seattle, WA, USA; [13]Novartis Pharmaceuticals Corporation, Detroit, MI, USA; [14]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [15]Novartis Pharmaceuticals Corporation, Basel, Switzerland; [16]Memorial Sloan Kettering Cancer Center, New York, NY, USA

KEY FINDINGS & CONCLUSIONS

- Despite higher incidences of haematologic TEAEs among participants with PSMA-positive mCRPC receiving ^{177}Lu-PSMA-617 versus ARPI change in PSMAfore, rates of complications or need for management of haematologic TEAEs were low and similar between treatment arms.
- Among participants who received 5–6 doses of ^{177}Lu-PSMA-617, TEAEs were more frequent at 1–4 doses than at 5–6 doses suggesting the risk of haematologic TEAEs does not increase.
- In both study treatment arms, participants with a higher number of bone metastases and lower SUV_{mean} at baseline had a higher rate of haematologic TEAEs.
  - This may be due to both off-target toxicity and disease-related factors.

Scan to obtain:
- Poster
- Supplementary material

https://bit.ly/KimNguye1611P

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INTRODUCTION

- In the phase 3 PSMAfore trial (NCT04689828) of [^{177}Lu]Lu-PSMA-617 (^{177}Lu-PSMA-617) in patients with metastatic castration-resistant prostate cancer (mCRPC), ^{177}Lu-PSMA-617 prolonged radiographic progression-free survival (rPFS) and had a favourable safety profile versus change of androgen receptor pathway inhibitor (ARPI).[1]
- ^{177}Lu-PSMA-617 has previously been associated with haematologic treatment-emergent adverse events (TEAEs).[2,3]
- The objective of this analysis was to assess the incidence, risk factors for and management of haematologic TEAEs for ^{177}Lu-PSMA-617 versus ARPI change in PSMAfore.

METHODS

- Eligible patients had prostate-specific membrane antigen (PSMA)-positive mCRPC, had not received taxane-based chemotherapy (except [neo]adjuvant ≥ 12 months ago) and were eligible for ARPI change after one progression on previous ARPI.
- Participants were randomized 1:1 to ^{177}Lu-PSMA-617 (7.4 GBq ± 10% every 6 weeks for six cycles) or ARPI change to abiraterone or enzalutamide.
- The primary endpoint was rPFS; secondary endpoints included frequency of TEAEs and safety laboratory assessments.
- Data are based on the third interim overall survival analysis of PSMAfore (data cutoff: 27 Feb 2024).
- Analyses were conducted in the safety set (all participants who received at least one dose of study treatment during the randomized treatment period).
- Haematologic TEAEs (Common Terminology Criteria for Adverse Events v5.0 coding) were grouped by Medical Dictionary for Regulatory Activities v26.1 terms; similar TEAEs as reported in the case report forms were combined for presentation purposes (participants were counted once per preferred term).
- Baseline metastatic bone disease was assessed by bone scan.
- [^{68}Ga]Ga-PSMA-11 mean standardized uptake value (SUV_{mean}) was calculated for the whole body.
- Median time to haematologic adverse events and median time to resolution of TEAEs were calculated using data from all participants with at least one event.
  - Time to resolution of TEAEs was defined as time from onset of event to date of first resolution.

RESULTS

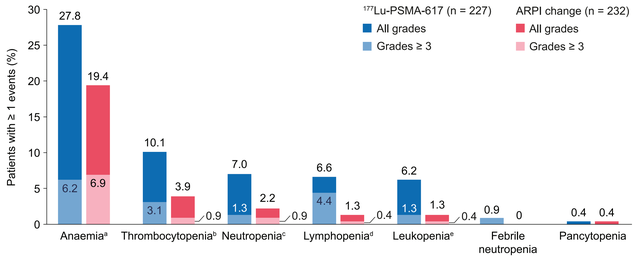
Patients

- The safety set comprised 227 participants randomized to ^{177}Lu-PSMA-617 and 232 participants randomized to ARPI change.
- The median time from randomization to the data cutoff (full analysis set) was 24.11 months (Q1, Q3: 20.24, 27.60) in the ^{177}Lu-PSMA-617 arm and 24.13 months (20.24, 27.37) in the ARPI change arm.

Overall haematologic TEAEs

- The incidence of haematologic TEAEs was higher among participants receiving ^{177}Lu-PSMA-617 (86/227 participants [37.9%]) than ARPI change (54/232 participants [23.3%]) (**Figure 1**).
  - TEAEs were mainly grade 1 or 2.
- Time to first occurrence of the most common haematologic TEAEs is shown in **Table 1**.

Figure 1. Incidence of haematologic TEAEs



Participants could be counted up to once per preferred term so could be counted more than once per TEAE grouping.
[a]Includes haemoglobin decreased. [b]Includes platelet count decreased. [c]Includes neutrophil count decreased. [d]Includes lymphocyte count decreased. [e]Includes white blood cell count decreased.
ARPI, androgen receptor pathway inhibitor; PSMA, prostate-specific membrane antigen; TEAE, treatment-emergent adverse event.

Table 1. Time to most common haematologic TEAEs

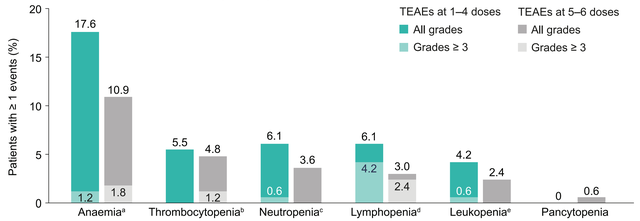
Median time to first occurrence of adverse event, weeks (Q1, Q3)	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)
Anaemia	n = 62 12.1 (2.3, 22.1)	n = 45 11.9 (4.1, 23.1)
Thrombocytopenia	n = 23 10.0 (3.3, 29.0)	n = 9 17.6 (12.7, 51.0)
Lymphopenia	n = 15 9.0 (2.0, 15.1)	n = 3 1.1 (0.1, 4.1)
Leukopenia	n = 25 11.9 (4.1, 16.1)	n = 6 8.1 (4.1, 21.1)

Time to neutropenia was not calculated.
Numbers of events used in the calculation of time to haematologic TEAE may differ from the number of TEAEs reported in **Figure 1** because the time to event analysis factors in related events to avoid underestimating the risk of interest.
ARPI, androgen receptor pathway inhibitor; PSMA, prostate-specific membrane antigen; TEAE, treatment-emergent adverse event.

Haematologic TEAEs by dose

- Among participants who received 5–6 doses of ^{177}Lu-PSMA-617, the incidence of haematologic TEAEs was higher at 1–4 doses (49/165 participants [29.7%]) than at 5–6 doses (33/165 participants [20.0%]) (**Figure 2**).

Figure 2. Incidence of haematologic TEAEs at 1–4 doses versus 5–6 doses of ^{177}Lu-PSMA-617 among participants who received 5–6 doses (n = 165)



Participants could be counted up to once per preferred term so could be counted more than once per TEAE grouping.
Participants could be counted up to once per dose category.
[a]Includes haemoglobin decreased. [b]Includes platelet count decreased. [c]Includes neutrophil count decreased. [d]Includes lymphocyte count decreased. [e]Includes white blood cell count decreased.
PSMA, prostate-specific membrane antigen; TEAE, treatment-emergent adverse event.

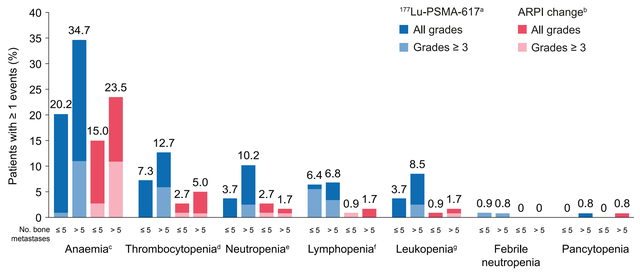
Haematologic TEAEs by baseline characteristics

- The incidence of any grade and grade ≥ 3 haematologic TEAEs was higher in participants with > 5 (^{177}Lu-PSMA-617: 53/118 participants [44.9%]; ARPI change: 32/119 participants [26.9%]) versus ≤ 5 (^{177}Lu-PSMA-617: 33/109 participants [30.3%]; ARPI change: 22/113 participants [19.5%]) bone metastases at baseline (**Figure 3**) and in participants with SUV_{mean} ≤ 10 (^{177}Lu-PSMA-617: 58/145 participants [40.0%]; ARPI change: 38/155 participants [24.5%]) versus > 10 (^{177}Lu-PSMA-617: 26/76 participants [34.2%]; ARPI change: 13/70 participants [18.6%]) at baseline (**Figure 4**).

Management of haematologic TEAEs

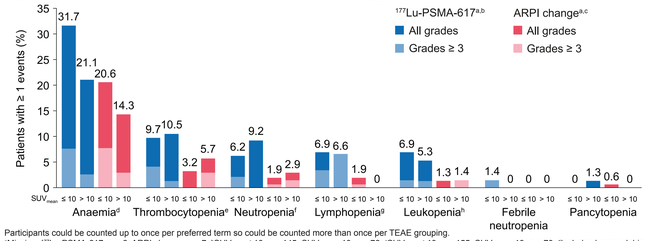
- The incidence of participants requiring blood product transfusions (on-treatment and during follow-up) was low in both arms (^{177}Lu-PSMA-617: 29/227 participants [12.8%]; ARPI change: 28/232 participants [12.1%]).
- For ^{177}Lu-PSMA-617 versus ARPI change, 4 participants (1.8%) versus 3 (1.3%) received erythropoietin and 3 (1.3%) versus 0 (0%) received granulocyte colony-stimulating factors.

Figure 3. Incidence of haematologic TEAEs by number of bone metastases on bone scan at baseline



Participants could be counted up to once per preferred term so could be counted more than once per TEAE grouping.
[a]≤ 5 bone metastases, n = 109; > 5 bone metastases, n = 118. [b]≤ 5 bone metastases, n = 113; > 5 bone metastases, n = 119. [c]Includes haemoglobin decreased. [d]Includes platelet count decreased. [e]Includes neutrophil count decreased. [f]Includes lymphocyte count decreased. [g]Includes white blood cell count decreased.
ARPI, androgen receptor pathway inhibitor; PSMA, prostate-specific membrane antigen; TEAE, treatment-emergent adverse event.

Figure 4. Incidence of haematologic TEAEs by baseline SUV_{mean}



Participants could be counted up to once per preferred term so could be counted more than once per TEAE grouping.
[a]Missing: ^{177}Lu-PSMA-617, n = 6; ARPI change, n = 7. [b]SUV_{mean} ≤ 10, n = 145; SUV_{mean} > 10, n = 76. [c]SUV_{mean} ≤ 10, n = 155; SUV_{mean} > 10, n = 70. [d]Includes haemoglobin decreased. [e]Includes platelet count decreased. [f]Includes neutrophil count decreased. [g]Includes lymphocyte count decreased. [h]Includes white blood cell count decreased.
ARPI, androgen receptor pathway inhibitor; PSMA, prostate-specific membrane antigen; SUV_{mean}, mean standardized uptake value; TEAE, treatment-emergent adverse event.

Time to resolution for haematologic TEAEs

- Time to resolution for key haematologic TEAEs is shown in **Table 2**.

Table 2. Time to resolution for key haematologic TEAEs

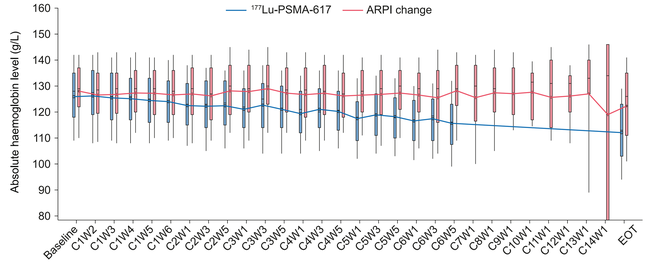
		^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)
Anaemia	n/m (%)	23/61 (37.7)	21/44 (47.7)
	Median time to resolution, months (Q1, Q3)	1.41 (0.39, 4.70)	0.92 (0.26, 2.73)
Thrombocytopenia	n/m (%)	9/17 (52.9)	1/7 (14.3)
	Median time to resolution, months (Q1, Q3)	0.92 (0.49, 5.82)	0.26 (0.26, 0.26)
Neutropenia	n/m (%)	9/13 (69.2)	2/2 (100.0)
	Median time to resolution, months (Q1, Q3)	1.38 (0.79, 4.96)	0.61 (0.26, 0.95)

Data include participants who received blood product transfusions.
ARPI, androgen receptor pathway inhibitor; n/m, number of patients with resolved event/number of patients with ≥ 1 event; PSMA, prostate-specific membrane antigen; TEAE, treatment-emergent adverse event.

Change in haematology parameters while on treatment

- Levels of haemoglobin (**Figure 5**), platelet, neutrophil and lymphocyte (**Figure S1**; available through the QR code) over time for the pooled ^{177}Lu-PSMA-617 and ARPI change arms are shown as box plots.
  - There were larger reductions in the levels of haematology parameters in the ^{177}Lu-PSMA-617 arm than in the ARPI change arm, consistent with the observed TEAEs shown in **Figure 1**.

Figure 5. Change in absolute haemoglobin levels from baseline to end of treatment



ARPI, androgen receptor pathway inhibitor; CXWX, cycle X week X; EOT, end of treatment; PSMA, prostate-specific membrane antigen.

References

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