8-year outcomes of enzalutamide (ENZA) versus a non-steroidal anti-androgen (NSAA) for metastatic, hormone-sensitive prostate cancer (ENZAMET; ANZUP 1304)

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1. Background and methods

- ENZAMET showed that enzalutamide (ENZA) plus testosterone suppression (TS) improved overall survival (OS) for metastatic hormone-sensitive prostate cancer (mHSPC) compared to non-steroidal anti-androgen (NSAA) plus TS. We now report the outcomes after a median follow-up of 98 months (>8 years)
- 1125 participants (pts) with mHSPC were randomly assigned (1:1) to enzalutamide (ENZA; 160 mg/day) or NSAA, plus TS

ENDPOINTS AND STATISTICAL ANALYSES

- **Primary endpoint:** OS was analysed using the Kaplan-Meier method, stratified log-rank, and stratified Cox regression
- **Secondary endpoints:** Deaths due to PC vs other causes were analysed using Fine and Gray regression and sub-distribution hazard ratios (sdHR) to account for competing risks

2. Baseline characteristics

Table 1: Baseline characteristics of ENZAMET

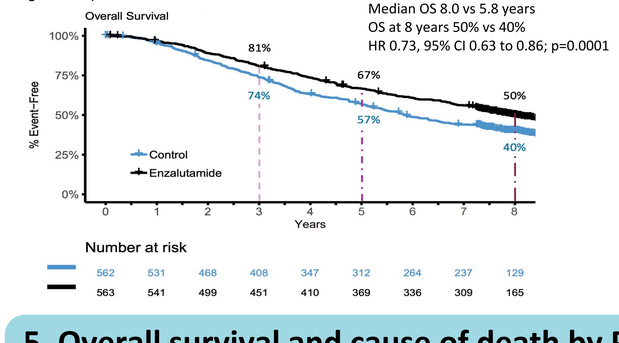
Baseline characteristics	TS + Enzalutamide (N=563)	TS + NSAA (N=562)
Age, median years (IQR)	69 (63-74)	69 (64 -75)
Synchronous metastases	60%	62%
Visceral metastases	12%	13%
Planned early docetaxel	45%	45%
Volume of disease		
High	54%	54%
Low	46%	46%

3. Results

- After a median follow-up of 8.1 years (IQR 7.7 to 8.9) and at data cut-off date 30JUN2024, 185/563 **(33%)** remain on **ENZA** and 79/562 **(14%)** on **NSAA**. Of those on ENZA, 88% remain on 160mg
- **Death** was reported in 285/563 **(51%)** pts assigned ENZA vs 337/562 **(60%)** assigned NSAA. **OS was longer** among those assigned **ENZA than NSAA** (Figure 1)
- **Clinical PFS** continued to **favour ENZA over NSAA** (HR=0.49; 95% CI 0.42 to 0.57; p<0.0001)

4. Overall survival

Figure 1: Updated overall survival results



5. Overall survival and cause of death by PSA ≤0.2 ng/mL at 7 months

Table 2: Deaths due to prostate cancer and due to other causes

	ENZA (N=563)	NSAA (N=562)
All participants		
Deaths due to prostate cancer, n	207	261
sdHR (95% CI)	sdHR 0.72, 95% CI 0.60 to 0.87	
Deaths due to other causes, n	78	76
sdHR (95% CI)	sdHR 1.24, 95% CI 1.06 to 1.45	
Participants with PSA ≤0.2 at 7 months		
8-year survival	56%	54%
8-year PC mortality rate	26%	31%
8-year non-PC mortality rate	13%	10%
Participants with PSA >0.2 at 7 months		
8-year survival	25%	22%
8-year PC mortality rate	57%	61%
8-year non-PC mortality rate	11%	14%

- The median baseline PSA was 8 ng/mL (IQR 2,33) in both treatment arms (NSAA and ENZA). 822/1125 (73%) of pts achieved PSA ≤0.2, with a **median time to PSA nadir of 5.4 months** (95% CI, 5.0-5.5). The median time to PSA ≤0.2 was **3.0 months** (95% CI 2.8 – 3.7) in **ENZA** vs. **5.6 months** (95% CI 5.5 – 6.1) in **NSAA**.
- 375/563 (67%) of pts assigned to ENZA achieved PSA at 7m ≤0.2 compared to 270/562 (48%) assigned to NSAA
- Compared with pts with PSA at 7m >0.2, **pts who achieved PSA ≤0.2 had significantly better survival probabilities** in both ENZA and NSAA arms (8-year survival probability 23% vs 55%; p<0.001; Figure 2)
- Among pts with PSA at 7m ≤0.2, deaths due to PC were seen in 29%. Deaths from other causes were seen in 13% of this subgroup and **accounted for 32% of the deaths** observed in this **better prognosis group**. Among pts with PSA at 7m >0.2, deaths due to PC occurred in 60%. Death from other causes were seen in 13% of this subgroup and accounted for **18% of deaths in this poor risk subgroup** (Figure 3)

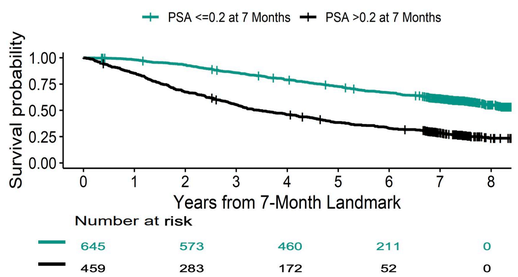


Figure 2: Overall survival by PSA ≤ 0.2 at 7 months

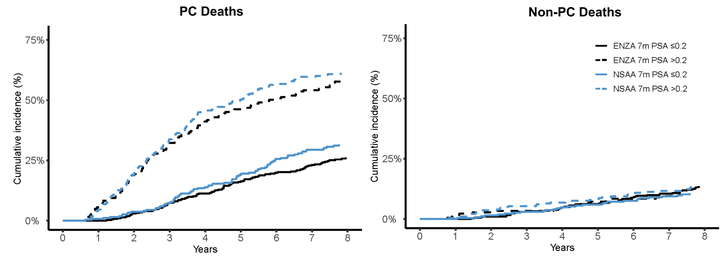


Figure 3: Prostate cancer and non-prostate cancer deaths by PSA at 7 months

Conclusions

After a median of follow-up of >8 years, overall survival remains statistically significant and clinically relevant for patients assigned enzalutamide plus TS compared to NSAA plus TS on the ENZAMET study

- Deaths due to prostate cancer were less frequent in those assigned ENZA vs. NSAA; deaths due to other causes occurred with the same frequency
- ENZA was associated with higher proportion of patients achieving PSA nadir ≤0.2 ng/mL at 7 months of therapy compared with NSAA
- Consistent with other datasets, PSA nadir at 7 months was a significant predictive factor of OS in patients with mHSPC, irrespective of treatment arm

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