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Health-related quality of life (HRQL) in a randomized phase 3 trial of enzalutamide with standard first line therapy for metastatic, hormone-sensitive prostate cancer (mHSPC)

ENZAMET (ANZUP 1304)
an ANZUP-led international cooperative group trial
(NHMRC CTC, CCTG, CTI, DFCI)

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HRQL in ENZAMET
Background and Methods

Enzalutamide (ENZA) versus an older (weaker) non-steroidal antiandrogen (NSAA), added to standard first line testosterone suppression, with or without concurrent early docetaxel, in mHSPC resulted in Davis et al, NEJM 2019

- longer clinical progression-free survival (hazard ratio 0.40, 95% CI, 0.33 to 0.49; p<0.001)
- longer overall survival (hazard ratio 0.67, 95% CI 0.52 to 0.86; p=0.002)

HRQL was a key secondary outcome assessed according to

- **EORTC QLQ-C30** and **PR25** at weeks 0, 4, 12, and then 12-weekly until clinical progression.
- differences in **least squares means** over 3 years (Mixed Model for Repeated Measures)
- differences in **deterioration-free survival** over 3 years (Kaplan-Meier method and log-rank test)
  - composite endpoint defined a priori as the earliest of
  - death, clinical progression, cessation of study treatment, or
  - a 10-point worsening from baseline (minimum clinically important difference on a 0-100 scale) in
  - Physical Function, Cognitive Function, Fatigue, or Global Health and quality of life

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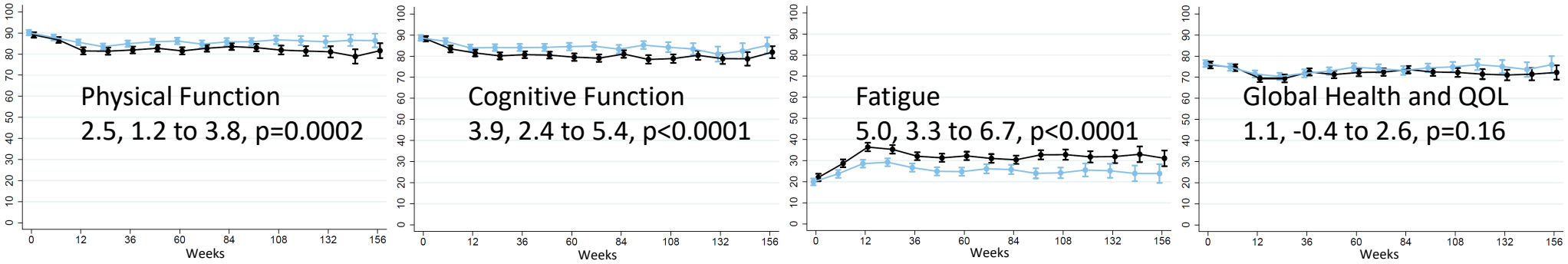
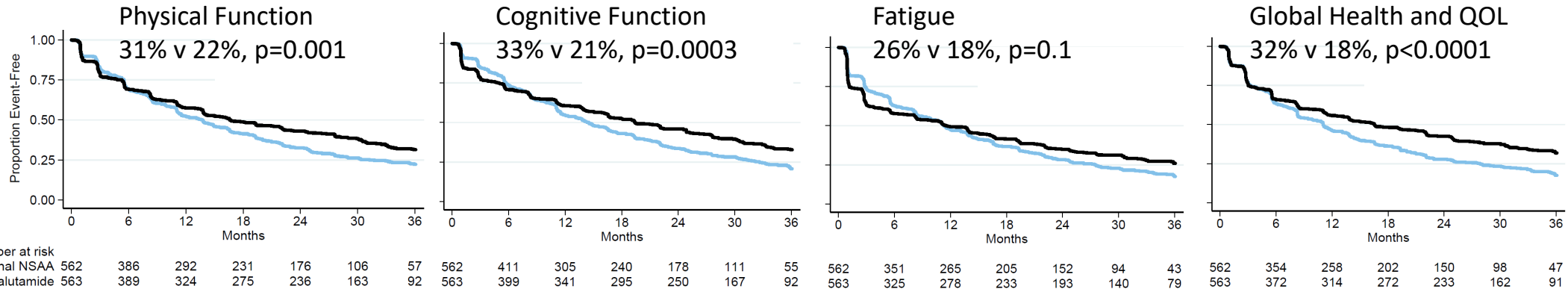
Effects of adding enzalutamide vs conventional NSAA on HRQL and deterioration-free survival

HRQL scores over time
least squares mean difference, 95% CI, p-value



Deterioration-free survival
percent deterioration-free at 3 years, log-rank p-value



Number at risk

Conventional NSAA	562	386	292	231	176	106	57	562	411	305	240	178	111	55	562	351	265	205	152	94	43	562	354	258	202	150	98	47
Enzalutamide	563	389	324	275	236	163	92	563	399	341	295	250	167	92	563	325	278	233	193	140	79	563	372	314	272	233	162	91

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HRQL in ENZAMET
Conclusions and Implications

The addition of ENZA (v NSAA) to testosterone suppression (± concurrent early docetaxel)

- maintained Global Health and Quality of Life
- improved deterioration-free survival because early impairments in specific aspects of HRQL were insufficient to outweigh subsequent benefits of delayed clinical progression.
- Was associated with deterioration-free survival benefits at 3 years that were smaller with early docetaxel than without it, but these differences were not beyond the play of chance

Enzalutamide added to testosterone suppression alone

- is an appropriate option for men with mHSPC starting testosterone suppression alone

For men who are candidates for docetaxel when starting testosterone suppression

- longer follow-up is needed to determine if the delays in progression and in time to deterioration with concurrent enzalutamide result in improved overall survival beyond 3 y

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In collaboration with: