Which patients with metastatic hormone-sensitive prostate cancer (mHSPC) benefit more from androgen receptor pathway inhibitors (ARPIs)?

STOPCAP meta-analysis of individual participant data

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ASCO Genitourinary Cancers Symposium #GU25

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Background and aims

- Clear evidence from large, high-quality trials that adding ARPI to standard care substantially improves outcomes

Aims of current analysis:

? Do effects vary between classes of ARPI?

? Do ARPI effects vary by patient or disease characteristics?

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Methods: design and outcomes

Design

- Pairwise meta-analysis of individual participant data (IPD) from completed trials

Outcomes

- Overall survival (OS): primary outcome for main effects
- Progression-free survival (PFS): primary outcome for subgroup analyses
  - ➢ To increase power, with OS as sensitivity
  - ➢ Defined as time to first clinical progression, radiological progression or death
- Prostate cancer specific survival (PCSS): sensitivity outcome

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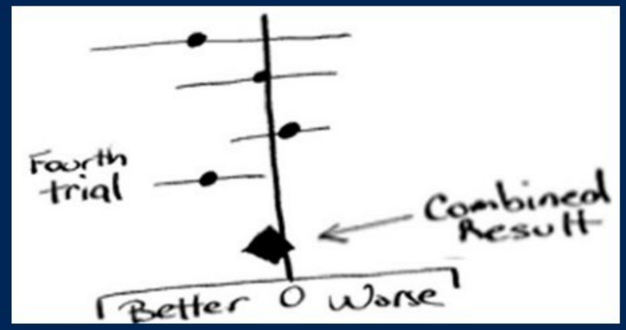
Methods: Analysis



- ITT, two-stage, fixed-effect IPD* meta-analysis of hazard ratios (HRs)
  - With pre-specified sensitivity analyses
- Adjusted for core set of covariates
  - Age, PSA, performance status, Gleason, timing of diagnosis
- Adjusted for trial-adaptive changes or protocol modifications
  - Docetaxel as part of standard care
- 5-year absolute differences from HRs and appropriate baseline rates

*IPD=individual participant data

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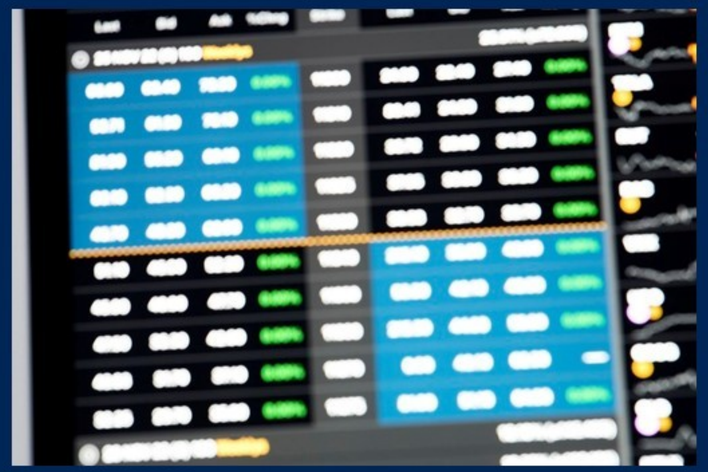
Results: Data available



Eligible: 11 ARPI trials; 11,154 patients

Available: 7 trials; 7,778 patients (70%)

- 4 trials of androgen biosynthesis inhibitors; 4,685 patients (100%)
  STAMPEDE (abi), LATITUDE (abi), PEACE-1 (abi), SWOG 1216 (ort)*
- 3 trials of “amides” ± abiraterone; 3,093 patients (48%)
  ENZAMET (enz), TITAN (apa), STAMPEDE (abi + enza)

* Included in sensitivity analyses only

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Results: Key patient characteristics

Trial ID	Synchronous	High volume	Median age (IQR)	Docetaxel as part of SOC	cT4*
STAMPEDE (abi)	94%	56%*	67 (62-71)	0%	28%
LATITUDE (abi)	100%	94%	65 (60-70)	0%	27%
PEACE-1 (abi)	100%	57%	67 (60-72)	61%†	19%
ENZAMET (enz)	68%*	54%	69 (64-75)	45%†	14%
TITAN (apa)	86%*	63%	65 (60-70)	11%‡	19%
STAMPEDE (abi+enz)	93%	53%*	69 (63-74)	9%§	26%
SWOG 1216 (ort)	Unknown	Unknown	68 (62-74)	0%	Unknown

* Some data unavailable

† Stratified by planned use of docetaxel

§ Stratified by use of docetaxel

‡ Stratified by prior use of docetaxel

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Results: Median follow-up and control-arm survival

Trial	No. of participants	Follow-up (years)	Survival (years)
STAMPEDE (abi)	1,003	8.0	3.8
LATITUDE (abi)	1,199	4.3	3.0
PEACE-1 (abi)	1,172	6.0	4.6
ENZAMET (enz)	1,125	5.7	6.1
TITAN (apa)	1,052	3.7	4.4
STAMPEDE (abi + enza)	916	6.0	4.3
SWOG 1216 (ort)	1,311	6.9	6.3

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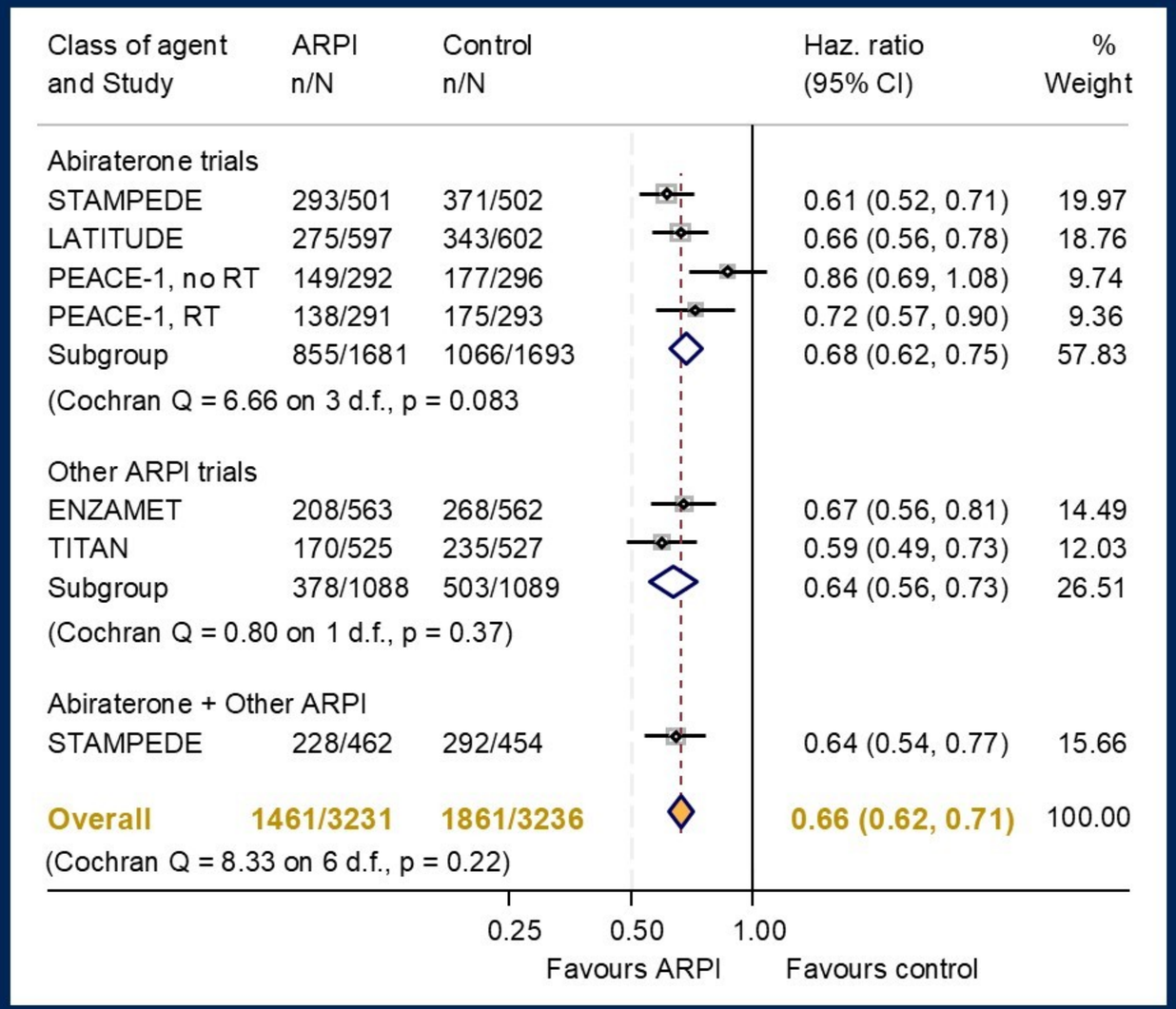
Effects of ARPIs on OS by class of agent



- Clear benefit of ARPIs on OS
  - ➢HR = 0.66 (CI 0.62 to 0.71)
  - ➢13% absolute improvement at 5 years
- Clear benefit of ARPIs on PFS
  - ➢HR = 0.51 (CI 0.48 to 0.55)
  - ➢21% absolute improvement at 5 years
- No clear difference by class of agent
  - ➢Based on 48% “amide” data

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Effects of ARPIs on PFS by patient & tumour characteristics

- No clear difference in the effects of ARPIs on PFS by
  - **Volume** of metastases
  - **Timing** of metastatic diagnosis
  - Clinical T-stage
  - Gleason sum score
  - Nodal involvement
  - Location of metastases
  - WHO performance status
  - BMI at randomisation
- Similar results for sensitivity analysis

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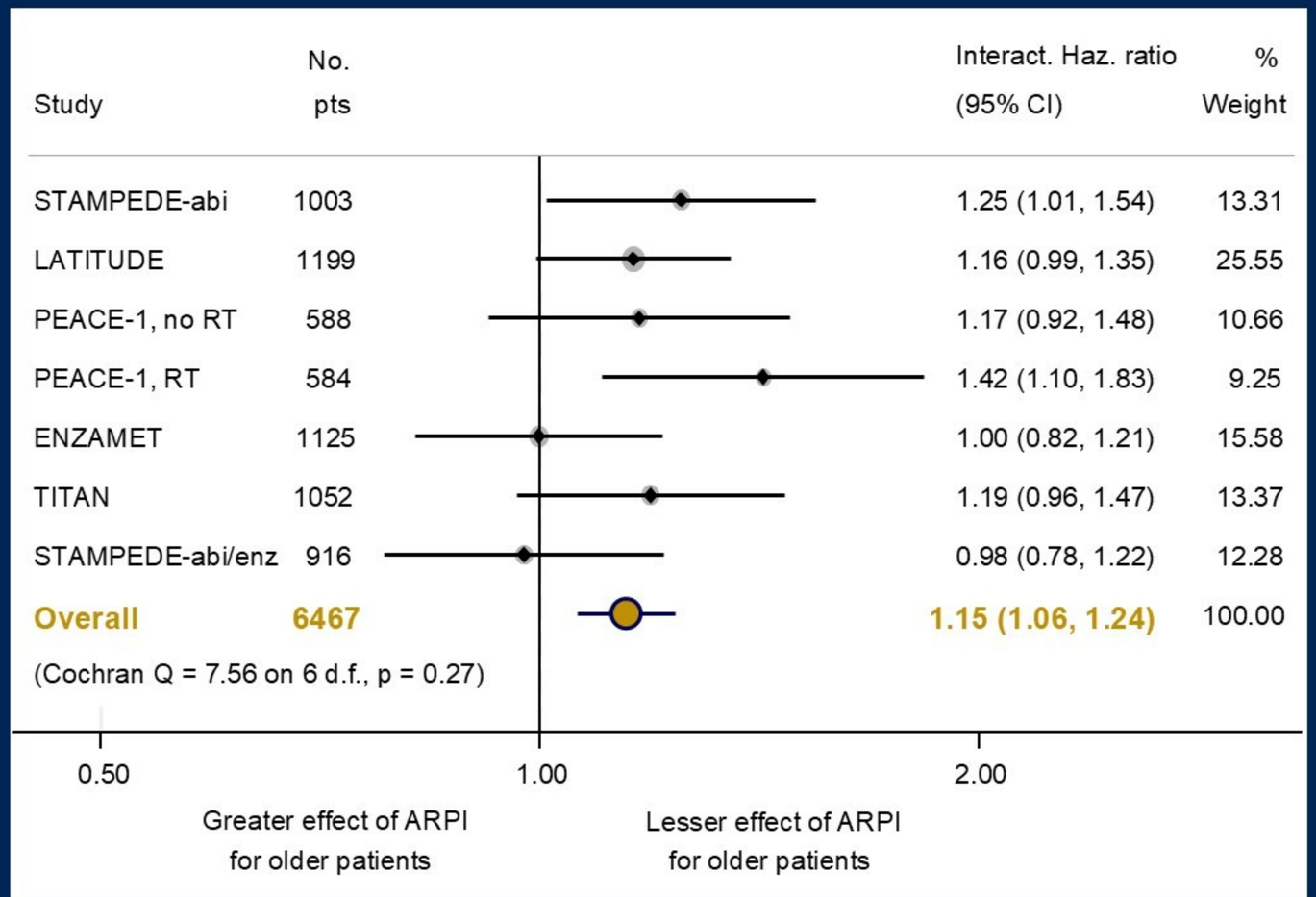
Effects of ARPIs on PFS by age



- Age not prognostic
- PFS effect decreases with increasing age
  - ➢Interaction HR=1.15 (CI 1.06-1.24)
- OS effect decreases with increasing age
  - ➢Interaction HR=1.11 (CI 1.01-1.21)

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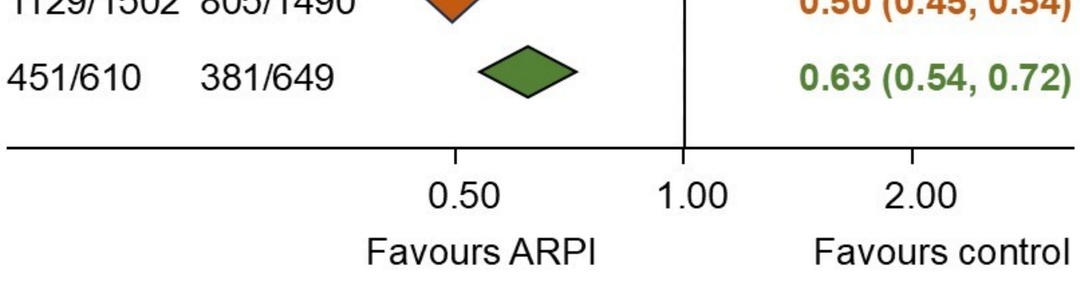
Effects of ARPIs by age group

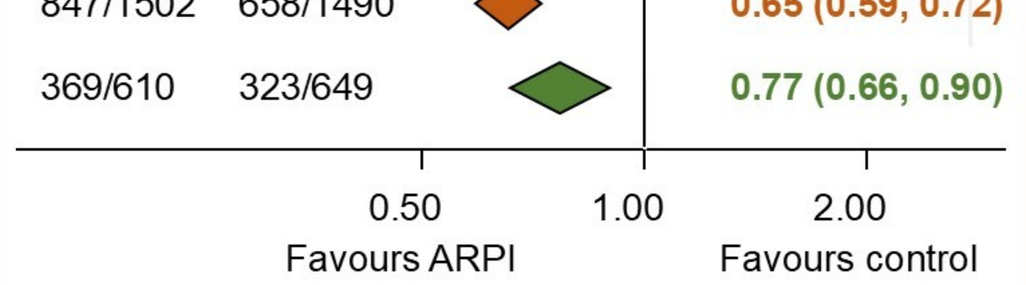
PFS

Age group	Control n/N	ARPI n/N	Haz. ratio (95% CI)
<65	872/1124	627/1092	0.47 (0.43, 0.53)
65 to <75	1129/1502	805/1490	0.50 (0.45, 0.54)
75+	451/610	381/649	0.63 (0.54, 0.72)



OS

Control n/N	ARPI n/N	Haz. ratio (95% CI)
645/1124	480/1092	0.63 (0.56, 0.71)
847/1502	658/1490	0.65 (0.59, 0.72)
369/610	323/649	0.77 (0.66, 0.90)



75+ vs <65: Interaction HR=1.32, p=0.003
Heterogeneity p=0.055

Interaction HR=1.22, p=0.052
Heterogeneity p=0.16

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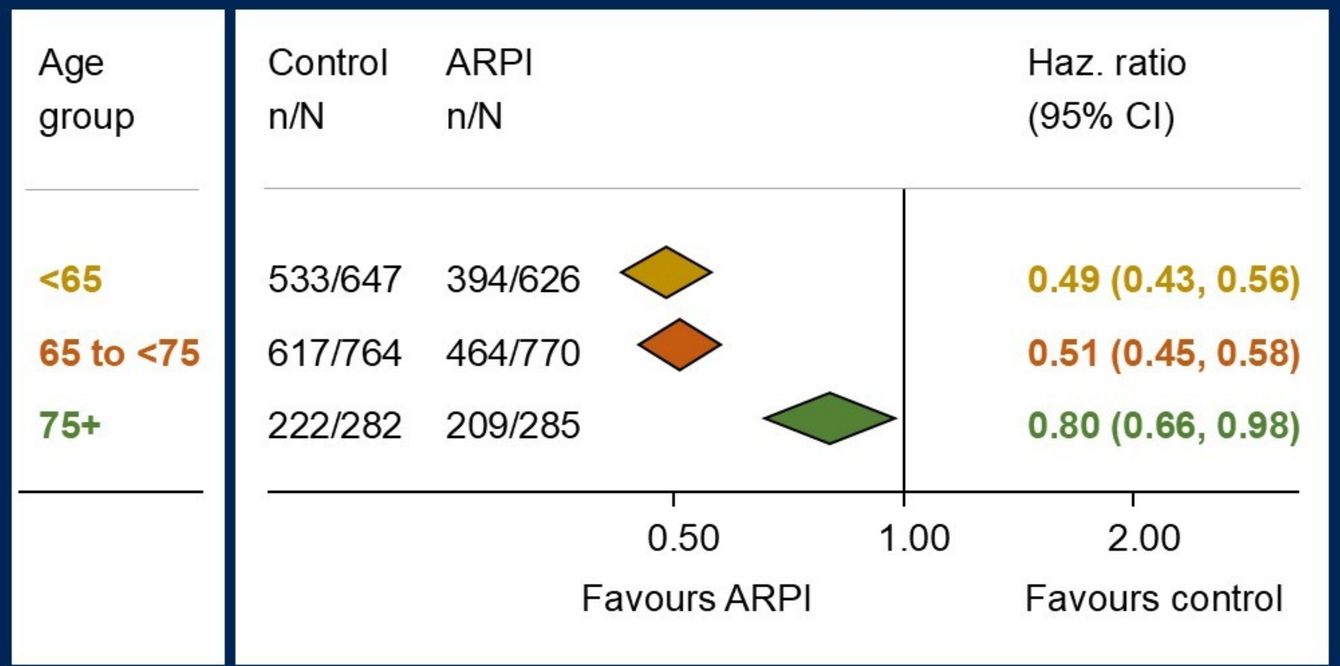
Effects of ARPI by age group: abiraterone trials

PFS



- 100% of data from eligible trials
  - STAMPEDE, LATITUDE, PEACE-1
- Complete outcome data

75+ vs <65: Interaction HR=1.64, p<0.001

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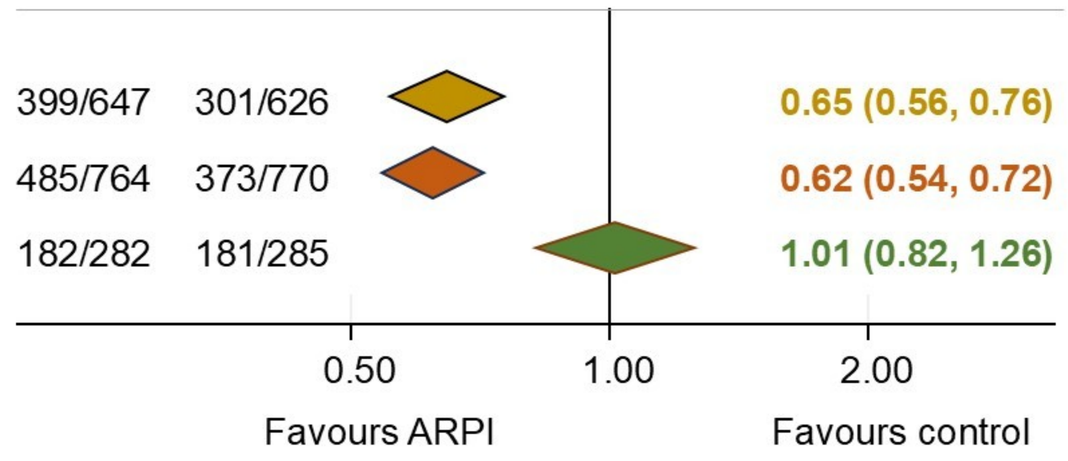
Effects of ARPIs by age group: abiraterone trials

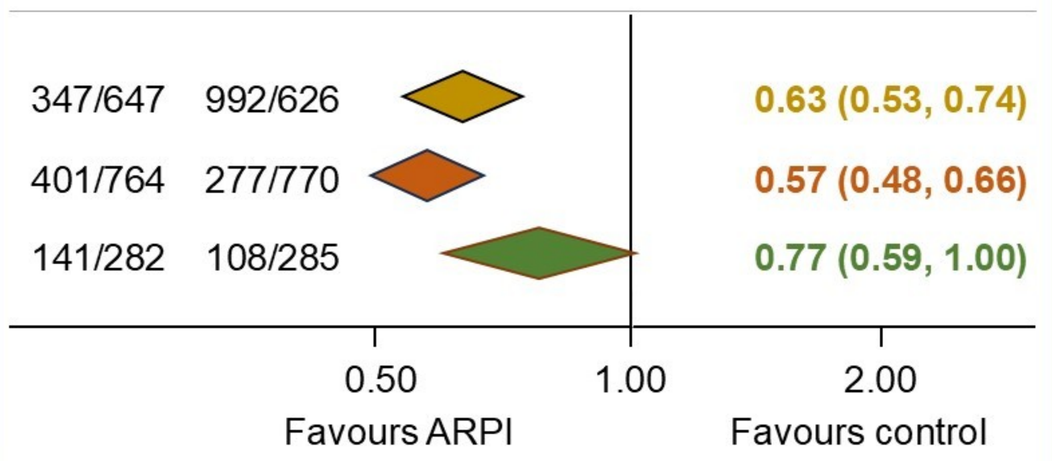
OS

Age group	Control n/N	ARPI n/N	Haz. ratio (95% CI)
<65	399/647	301/626	0.65 (0.56, 0.76)
65 to <75	485/764	373/770	0.62 (0.54, 0.72)
75+	182/282	181/285	1.01 (0.82, 1.26)



PCSS*

Control n/N	ARPI n/N	Haz. ratio (95% CI)
347/647	992/626	0.63 (0.53, 0.74)
401/764	277/770	0.57 (0.48, 0.66)
141/282	108/285	0.77 (0.59, 1.00)



75+ vs <65: Interaction HR=1.56, p=0.001

Interaction HR=1.23, p=0.19

*PCSS=prostate cancer-specific survival

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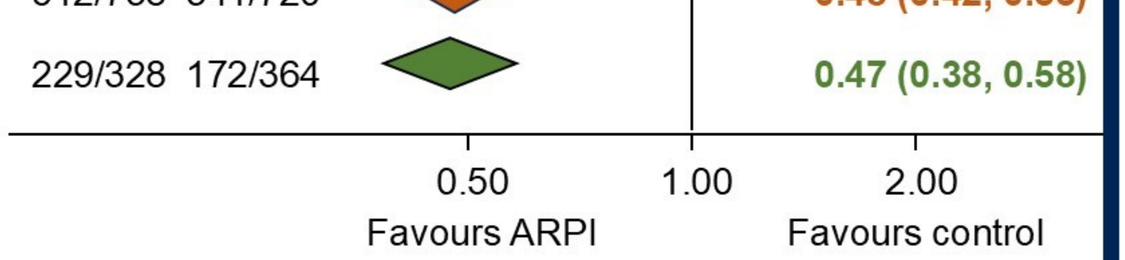
Effects of ARPIs by age subgroup: "amide" trials

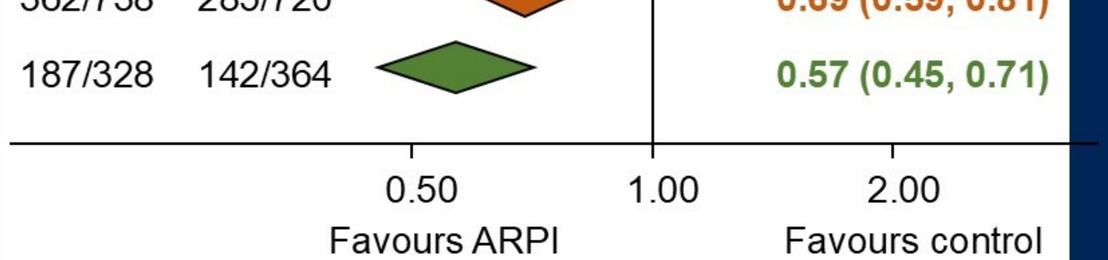
PFS

Age group	Control n/N	ARPI n/N	Haz. ratio (95% CI)
<65	339/477	233/466	0.46 (0.39, 0.55)
65 to <75	512/738	341/720	0.48 (0.42, 0.55)
75+	229/328	172/364	0.47 (0.38, 0.58)



OS

Control n/N	ARPI n/N	Haz. ratio (95% CI)
246/477	179/466	0.61 (0.50, 0.75)
362/738	285/720	0.69 (0.59, 0.81)
187/328	142/364	0.57 (0.45, 0.71)



75+ vs <65: Interaction HR=1.02, p=0.88 Interaction HR=0.93, p=0.61

Note: 48% available data at present

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5-year absolute effects of ARPIs, by age group

		PFS	OS	PCSS*
Younger age groups (<75)	Abiraterone trial data	~25%	~16%	~17%
	Amide (± abi) trial data	~27%	~18%	?
Oldest age group (75+)	Abiraterone trial data	~8%	~0%	~9%
	Amide (± abi) trial data	~27%	~19%	?

*PCSS=prostate cancer-specific survival

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Next steps

- Obtain more and better data
  - IPD* from ARCHES, ARASENS and ARANOTE trials
  - Longer follow-up, and complete cause-of-death data
  - Ability to download IPD* from YODA, Vivli and other repositories
- For thorough analysis of how agent and patient factors inter-relate
- To better understand results and maximise clinical insight

*IPD=individual participant data

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Strengths

STOPCAP international collaborative effort

70% IPD* across all eligible trials (7,778 participants)

100% of IPD* from abiraterone trials; 48% IPD* from other ARPI trials

More reliable & thorough than meta-analyses based on summary data

*IPD=individual participant data

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Key takeaways

- Clear benefit of ARPIs on OS & PFS for majority of mHSPC patients
- For younger patients, clear benefit from all ARPIs
- For older patients, consider benefits/risks of abiraterone and “amides”
- First meta-analysis of individual participant data from ARPI trials

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YODA for providing LATITUDE & TITAN trial data

This study, carried out under YODA Project #2019-4134/2024-0652, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C.. The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.. The original proposal can be found: https://yoda.yale.edu/data-request/2024-0652/.

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Acknowledgements

- STOPCAP core team
- STOPCAP international Advisory Group
- Trial teams, for providing data
- Participants' contribution to these trials
- Patient research partners
- UK Medical Research Council & Prostate Cancer UK funding

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FUNDED BY PROSTATE CANCER UK

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