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MEETING SUMMARY
PROSTATE CANCER HIGHLIGHTS FROM ESMO 2022

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PRACTICE-CHANGING DATA ESMO 2022

DURATION OF ADT WITH POST-OPERATIVE RT FOR PROSTATE CANCER: FIRST RESULTS OF THE RADICALS-HD TRIAL (ISRCTN40814031)

Parker C, et al. ESMO 2022. Abstract #LBA9

ADT, androgen deprivation therapy; RT, radiotherapy

RADICALS-HD: BACKGROUND AND STUDY DESIGN

- There is good evidence on the use of ADT with primary radiotherapy as initial treatment for prostate cancer
- By contrast, there is uncertainty about the role and duration of ADT with RT after radical prostatectomy

Inclusion Criteria

- Due for post-op RT after radical prostatectomy for adenocarcinoma

Exclusion Criteria

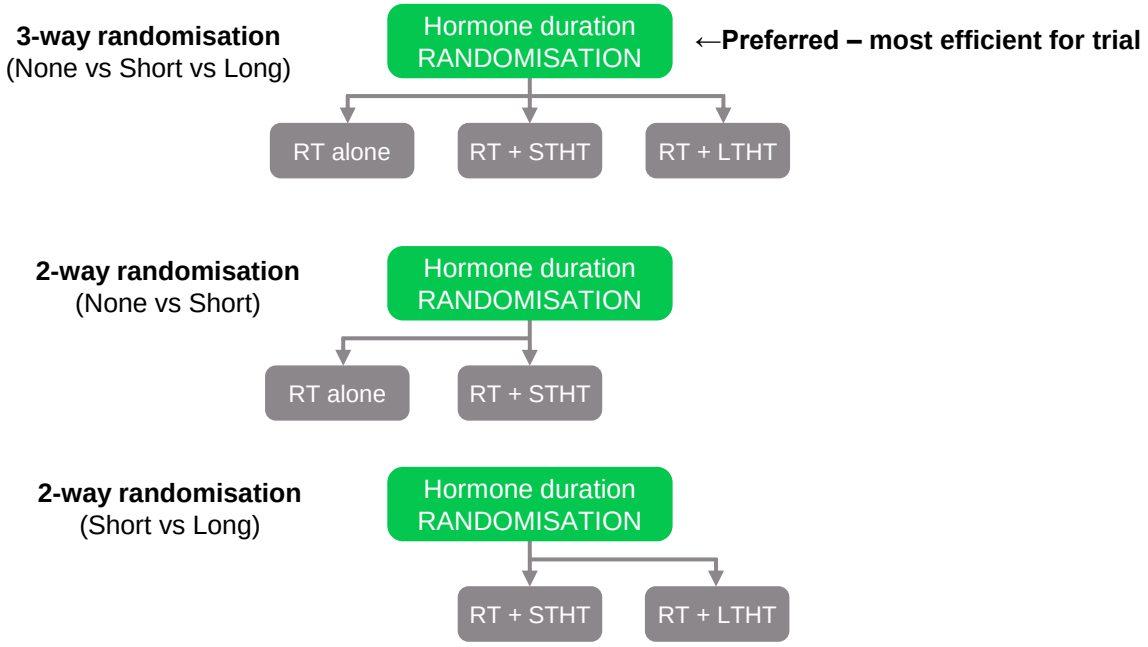
- Prior pelvic RT
- Prior hormone therapy
- Metastatic disease
- PSA >5 ng/mL

Primary Endpoint

- Metastasis-free survival (MFS)

Secondary Endpoint

- Time to salvage ADT
- Overall survival
- Toxicity



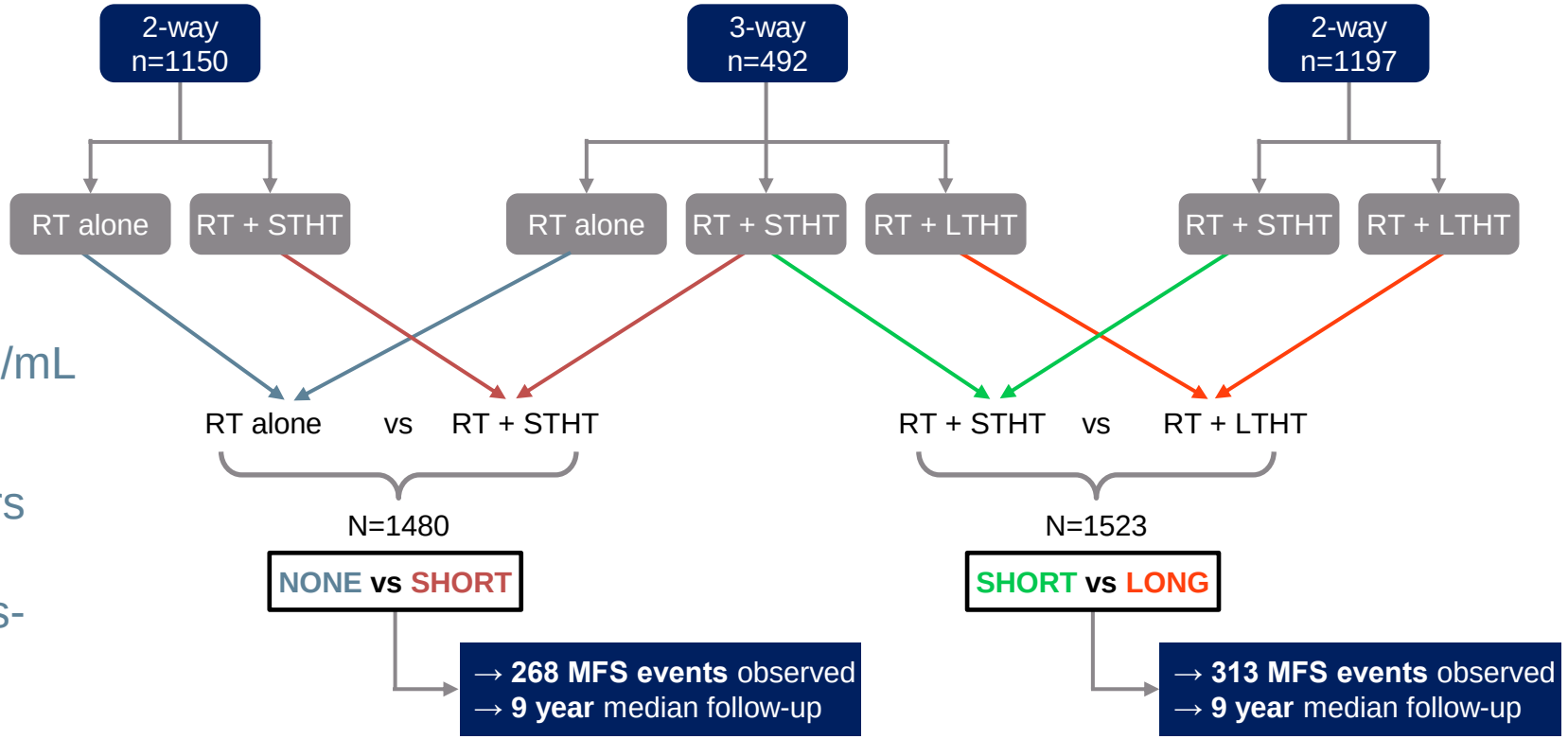
ADT, androgen deprivation therapy; LTHT, long term hormone therapy; MFS, metastasis-free survival; PSA, prostate specific antigen; RT, radiotherapy; STHT, short term hormone therapy

Parker C, et al. Ann Oncol. 2022;33 (suppl_7):S808-S869 (ESMO 2022, oral presentation)

RADICALS-HD: PATIENT CHARACTERISTICS

- From 2007 to 2015, 2839 pts (inc. 492 in the 3-way randomisation) joined RADICALS-HD
- Median age: 66 years; 23% pT3b/T4; 20% Gleason 8-10; median pre-RT PSA 0.22 ng/mL
- Arms were balanced within each comparison; risk factors were more favourable in None-vs-Short than Short-vs-Long. Median follow-up was 9 years

Recruitment and randomisation



LTHT, long term hormone therapy; MFS, metastasis-free survival; PSA, prostate specific antigen; pt, patient; RT, radiotherapy; STHT, short term hormone therapy

Parker C, et al. Ann Oncol. 2022;33 (suppl_7):S808-S869 (ESMO 2022, oral presentation)

RADICALS-HD: RESULTS

NONE VS SHORT ANALYSIS	RT alone N=737	RT + STHT N=743
MFS		
Events, n	142	126
HR (95% CI), p-value	0.89 (0.69-1.14), p=0.35	
10 yr event free, %	79	80
Time to salvage HT		
Events, n	176	109
HR (95% CI), p-value	0.54 (0.42-0.70), p<0.0001	
10 yr event free, %	73	82
OS		
Events, n	98	92
HR (95% CI), p-value	0.88 (0.65-1.19), p=0.42	
10 yr event free, %	86	85

SHORT VS LONG ANALYSIS	RT + STHT N=761	RT + LTHT N=762
MFS		
Events, n	174	139
HR (95% CI), p-value	0.77 (0.61-0.97), p=0.03	
10 yr event free, %	72	78
Time to salvage HT		
Events, n	200	157
HR (95% CI), p-value	0.73 (0.59-0.91), p=0.005	
10 yr event free, %	69	75
OS		
Events, n	111	100
HR (95% CI), p-value	0.88 (0.66-1.17), p=0.38	
10 yr event free, %	82	85

- Radiotherapy toxicity was assessed using the RTOG scale – no significant differences were found between arms

CI, confidence interval; HR, hazard ratio; HT, hormone therapy; LTHT, long term hormone therapy; MFS, metastasis-free survival; OS, overall survival; RT, radiotherapy; RTOG, Radiation Therapy Oncology Group; STHT, short term hormone therapy; yr, year

Parker C, et al. Ann Oncol. 2022;33 (suppl_7):S808-S869 (ESMO 2022, oral presentation)

RADICALS-HD: SUMMARY

- In pts having post-operative RT after RP, 24 mo ADT vs 6 mo ADT improved both time to salvage ADT and MFS
  - In contrast, 6 mo ADT vs no ADT improved time to salvage ADT but did not improve MFS
- Overall survival was not improved (HR 0.88, 95% CI 0.66-1.17) with 6 mo ADT vs 24 mo ADT
- 6 months of ADT versus no ADT improved time to salvage ADT but not MFS

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; MFS, metastasis-free survival; mo, months; PSA, prostate specific antigen; RP, radical prostatectomy; RT, radiotherapy; pt, patients

Parker C, et al. Ann Oncol. 2022;33 (suppl_7):S808-S869 (ESMO 2022, oral presentation)

DURATION OF ANDROGEN SUPPRESSION WITH POST-OPERATIVE RADIOTHERAPY (DADSPORT): A COLLABORATIVE META-ANALYSIS OF AGGREGATE DATA

Burdett S, et al. ESMO 2022. Abstract #LBA64

DADSPORT: BACKGROUND AND STUDY DESIGN

- The **DADSPORT** collaboration conducted a systematic review and meta-analysis of results from NRG/RTOG 9601, GETUG-AFU 16, NRG/RTOG 0534, and the newly-available, RADICALS-HD trials to assess the effect of hormone therapy in men receiving radiotherapy following radical prostatectomy for localised prostate cancer

Trial	Accrual period	Number of men	Duration of HT
GETUG-AFU 16 (Carrie et al. 2016, 2019	2006-2010	743	None vs 6m
NRG/RTOG 0534 (Pollack et al. 2022	2008-2015	1142	None vs 6m
NRG/RTOG 9601 (Shipley et al. 2017, Dess et al. 2020)	1998-2003	760	None vs 24m
RADICALS-HD (Unpublished)	2007-2015	2839	None vs 6m None vs 6m vs 24m 6m vs 24m

3 trial comparisons – Non vs 6m HT, 3364 men
2 trial comparisons – None vs 24m HT, 1088 men

Trial level analyses
- No HT vs HT

Planned duration of HT
- No HT vs 6m HT
- No HT vs 24m HT

OUTCOMES
Primary outcome: OS
Secondary outcomes: MFS, PCSS

- **Does hormone therapy after radiotherapy offer an advantage over radiotherapy alone for those diagnosed with localised prostate cancer?**

HT, hormone therapy; m, months; MFS, metastasis-free survival; OS, overall survival; PCSS, prostate cancer specific survival

Burdett S, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation)

DADSPORT: RESULTS

OVERALL SURVIVAL

Treatment comparison	No. of trials included	No. of events/men	Hazard ratio (HR) (95% CI), p-value	Heterogeneity I^2, p-value
HT (any duration) vs no HT	4	701/4452	0.89 (0.77-1.03), p=0.13	I^2=0, p=0.42
HT (any duration) vs no HT: Sensitivity analysis	4	650/4334	0.93 (0.80-1.08), p=0.35	I^2=0, p=0.67
6m HT vs no HT	3	419/3364	0.90 (0.74-1.09), p=0.28	I^2=0, p=0.98
24m HT vs no HT	2	282/1088	0.89 (0.72-1.10), p=0.29	I^2=74%, p=0.05
24m HT vs no HT: Sensitivity analysis	2	231/970	0.98 (0.78-1.23), p=0.87	I^2=49%, p=0.16

Median follow up ≥8 yrs; Sensitivity analysis excluded men with PSA > 1.5 ng/mL

METASTASIS-FREE SURVIVAL

- Data on MFS from 2 trials of 24m HT vs no HT are not yet available
- Based on data from 3 trials (653 events, 3364 men; 100%), there was evidence that 6m HT improved MFS compared to no HT (HR 0.82, 95% CI 0.70-0.96, p=0.013)

CI, confidence interval; HR, hazard ratio; HT, hormone therapy; m, months; MFS, metastasis-free survival; OS, overall survival

Burdett S, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation)

DADSPORT: SUMMARY

- No clear evidence of difference in survival with either 6 or 24 months of hormone therapy versus none
- Evidence of improved MFS with 6 months hormone therapy compared to no hormone therapy

Clinical Perspective

- **Is salvage after radiotherapy needed? Probably but not always.**
  If yes when? As early as possible. If ADT is added, the benefit is in improved metastases free survival (6 months) with no OS benefit after ≥ 8 years of follow-up

ADT, androgen-deprivation therapy; MFS, metastasis-free survival; OS, overall survival

Burdett S, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation); Mottet N. Discussant of abstract #LBA64, ESMO 2022.

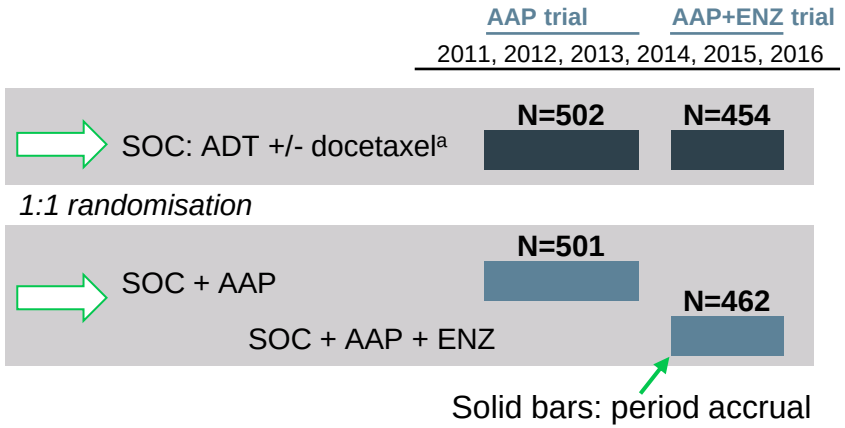
COMPARISON OF AAP OR COMBINATION ENZ + AAP FOR mHSPC STARTING ADT: OS RESULTS OF 2 RANDOMISED PHASE 3 TRIALS FROM THE STAMPEDE PROTOCOL

Attard G, et al. ESMO 2022. Abstract #LBA62

AAP, abiraterone acetate and prednisolone/prednisone; ADT, androgen deprivation therapy; ENZ, enzalutamide; mHSPC, metastatic hormone sensitive prostate cancer; OS, overall survival

STAMPEDE: BACKGROUND AND STUDY DESIGN

- Abiraterone acetate and prednisolone (AAP) or enzalutamide (ENZ) added to ADT improves outcomes for mHSPC patients[1,2]
- Combining ENZ and AAP may improve rPFS in mCRPC but there is no notable improvement in OS[3]
- The benefit in mHSPC is uncertain and survival outcomes of mPC started on ADT + second generation hormonal agent after >5 years have not been reported[4]



- No overlapping controls
- Same protocol & eligibility criteria
- 1[ary] outcome measure: OS[b]
- Aim: report effect of AAP+ENZ and then indirectly compare with AAP and with ENZ (other trials)

- Trial follow-up was based on funding availability
- Fixed-effects individual patient data meta-analyses to pool estimates from both trials and test for evidence of differences in treatment effect & in-between trial heterogeneity
- Both trials closed to further trial data collection, 30 Nov 2021
- Final data freeze, 3 July 2022

[a] docetaxel allowed **prior** to AAP+ENZ from Jan 2016
Daily doses: AA (1000mg) + P (5mg); ENZ 160mg
[b] Secondary outcome measures as reported previously

ADT, androgen deprivation therapy; mCRPC; metastatic castration resistant prostate cancer; mHSPC, metastatic hormone sensitive prostate cancer; mPC, metastatic prostate cancer; OS, overall survival; P, prednisolone/prednisone; rPFS, radiographic progression-free survival; SOC, standard of care

1. James ND, et al. N Engl J Med 2017; 377: 338-351; 2. David ID, et al. N Engl J Med 2019; 381: 121-131; 3. Morris MJ, et al. J Clin Oncol 2019; 37 (15 Suppl): 5008; 4. Attard G, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation)

STAMPEDE: RESULTS

EFFICACY

Endpoint	AAP Trial	AAP + ENZ trial	Interaction / Heterogeneity
Overall survival	HR 0.62 95% CI: 0.53-0.73 $p=1.6 \times 10^{-9}$	HR 0.65 95% CI: 0.55-0.77 $p=1.4 \times 10^{-6}$	HR 1.05 95% CI: 0.83-1.32 P=0.71 Between trial heterogeneity I^2 p=0.7
Metastatic PFS	HR 0.50 95% CI: 0.43-0.58	HR 0.52 95% CI: 0.44-0.62	No evidence of a difference in treatment effect or between trial heterogeneity

- **OS subgroup analysis for docetaxel:**
  - non-statistically significant interaction for effect (HR 0.81, 95% CI: 0.50-1.32, p=0.384)
- **At 7 years in AAP trial:**
  - 30% (95% CI: 26-34) patients were alive with ADT vs 48% (95% CI: 43-52) with ADT + AAP; median follow-up: 95.8 mo
  - Restricted mean survival times were 50.4 months with ADT alone versus 60.6 months with ADT + AAP ($p=6.6 \times 10^{-9}$)

SAFETY

Percentage of patients reporting **grade 3-5 toxicity** in the first 5-years was as follows:

- **AAP trial:**
  - ADT alone: 38.5%, 95% CI: 34.2-42.8
  - AAP: 54.4%, 95% CI: 50.0-58.8
- **AAP + ENZ trial:**
  - ADT alone: 45.2%, 95% CI: 40.6-49.8
  - AAP + ENZ: 67.9%, 95% CI: 63.5-72.2
- Toxicity with AAP + ENZ same as AAP but AEs occurred more frequently
- Most frequent AEs were fatigue, liver derangement and hypertension
- Of note were the higher incidence of G5 cardiac AEs in the AAP + ENZ treated patients and respiratory AEs in the AAP treated patients

AAP, Abiraterone acetate and prednisolone/prednisone; ADT, androgen deprivation therapy; AE, adverse event; CI, confidence interval; ENZ, enzalutamide; G, grade; HR, hazard ratio; mo, month; OS, overall survival; PFS, progression-free survival

Attard G, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation)

STAMPEDE: SUMMARY

- Enzalutamide + abiraterone acetate and prednisolone should not be combined for mHSPC (nor for high-risk localized prostate cancer)
- Clinically important improvements in OS when adding abiraterone acetate and prednisolone to ADT are maintained at 7 years

Clinical Perspective

- **ENZ plus AAP does not improve OS in *de novo* mHSPC and results in increased toxicity**

AAP, abiraterone and prednisolone/prednisone; ADT, androgen deprivation therapy; ENZ, enzalutamide; mHSPC, metastatic hormone sensitive prostate cancer; OS, overall survival

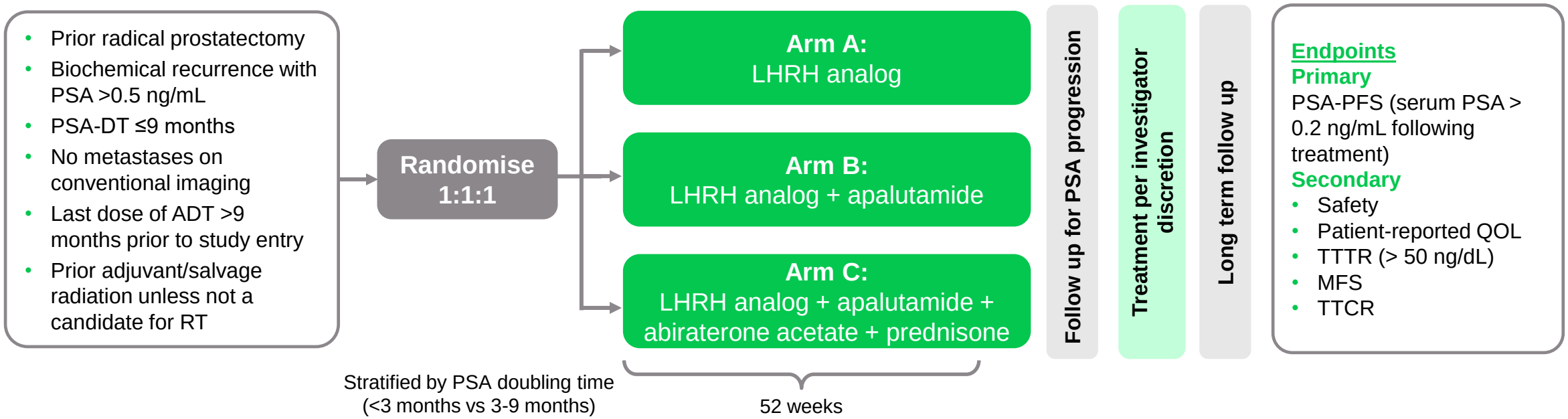
Attard G, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation); Castro E. Discussant of abstract #LBA62, ESMO 2022.

PRESTO: A PHASE 3, OPEN-LABEL STUDY OF ANDROGEN ANNIHILATION IN PATIENTS WITH HIGH-RISK BIOCHEMICALLY RELAPSED PROSTATE CANCER (AFT-19)

Aggarwal R, et al. ESMO 2022. Abstract #LBA63

PRESTO: BACKGROUND AND STUDY DESIGN

- Patients with biochemically relapsed prostate cancer following radical prostatectomy and a short PSA doubling time are at risk for distant metastases
- Apalutamide and abiraterone acetate plus prednisone prolong survival in the metastatic setting
- PRESTO evaluated if intensification of ADT prolongs biochemical PFS in BRPC



AAP, Abiraterone acetate plus prednisone; ADT, androgen deprivation therapy; BCR, biochemically recurrent; bPFS, biochemical progression free survival; BRPC, biochemically relapsed prostate cancer; LHRH, luteinising hormone-releasing hormone; MFS, metastasis free survival; PFS, progression-free survival; PSA, prostate specific antigen; PSA-DT, PSA-doubling time; QoL, quality of life; RT, radiotherapy; TTCR, time to castration resistance; TTTR, time to testosterone recovery

Aggarwal R, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation)

PRESTO: RESULTS

- 504 pts were randomized to ADT alone (N=167), ADT + APA (N = 168) or ADT + APA + AAP (N=169)

		ADT	ADT + APA	ADT + APA + AAP	HR (95% CI)
PSA-PFS	ARM B Comparison	20.3 mo (95% CI: 18.2-22.9)	24.9 mo (95% CI: 23.3-32.3)	–	0.52 (95% CI: 0.35-0.77) P=0.00047
	ARM C Comparison	20.0 mo (95% CI: 18.2-22.5)	–	26.0 mo (95% CI: 22.9-32.5)	0.48 (95% CI: 0.32-0.71) P=0.00008
TTTR	ARM B Comparison	4.0 mo	3.9 mo	–	0.96 (85% CI: 0.70-1.32)
	ARM C Comparison	4.0 mo	–	4.8 mo	0.80 (95% CI: 0.58-1.10)

102 events in total for PSA PFS; Median follow up for arm B comparison 21.5 months and 21.3 months for arm C

- Most common grade ≥2 AE was hypertension (19.4%, 23.4%, 30.4% in ADT, ADT + APA and ADT + APA + AAP arms, respectively)
- Eight pts (1.8%) across all treatment arms stopped treatment for AEs

AAP, abiraterone acetate plus prednisone; ADT, androgen deprivation therapy; AE, adverse event; APA, apalutamide; CI, confidence interval; HR, hazard ratio; mo, months; PSA-PFS, prostate specific antigen-progression free survival; TTTR, time to testosterone recovery

Aggarwal R, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation)

PRESTO: SUMMARY

- More complete AR blockade with APA in addition to ADT prolongs PSA-PFS with a manageable safety profile, without impacting TTTR following a finite duration of treatment
- More hypertension was seen in the AAP-containing treatment arm
- There does not appear to be further benefit with the addition of abiraterone + prednisone to apalutamide

Clinical Perspective

- **There is insufficient data at this point in time, to prescribe apalutamide, or abiraterone and apalutamide, for M0 HSPC with rising PSA, post-radical prostatectomy**
- **Additionally, this is a shrinking disease space due to PSMA PET, as well as the increased utilisation of SABR**

AAP, abiraterone acetate plus prednisone; ADT, androgen deprivation therapy; APA, apalutamide; AR, androgen receptor; M0 HSPC, non-metastatic hormone sensitive prostate cancer; PSA, prostate specific antigen; PSA-PFS, PSA-progression-free survival; PSMA PET, prostate specific membrane antigen positron emission tomography; SABR, Stereotactic ablative radiotherapy; TTTR, time to testosterone recovery

Aggarwal R, et al. Ann Oncol. 2022;33 (suppl_7): S808-S869 (ESMO 2022, oral presentation); de Bono J. Discussant of abstract #LBA63, ESMO 2022.

OTHER NOTEWORTHY PRESENTATIONS ESMO 2022

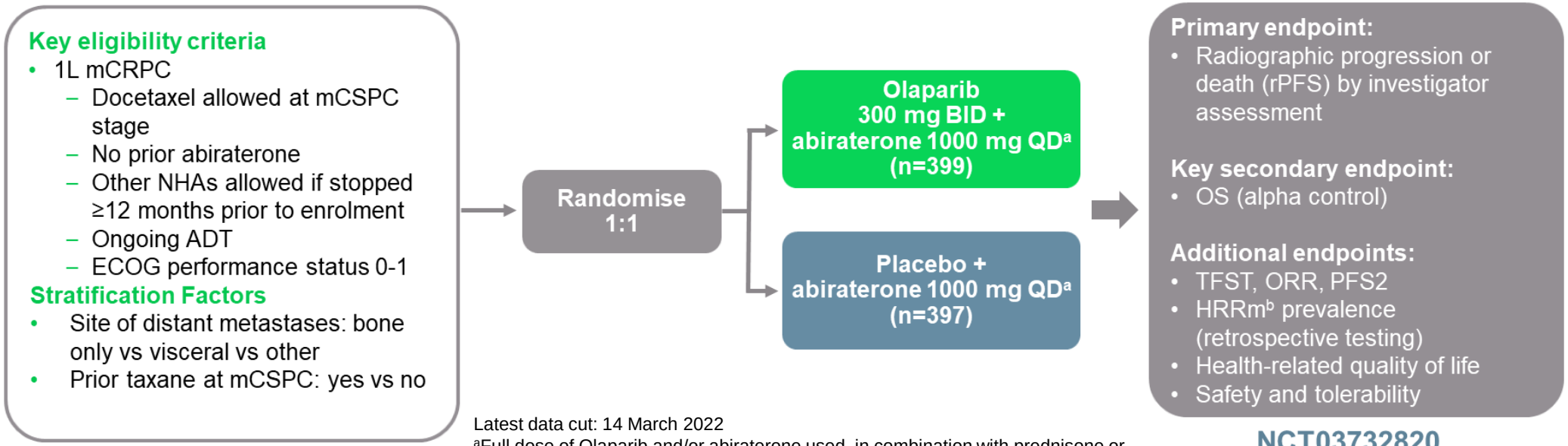
BIOMARKER ANALYSIS AND UPDATED RESULTS FROM THE PHASE 3 PROpel TRIAL OF ABI AND OLA VS ABI AND PBO AS 1L THERAPY FOR PTS WITH mCRPC

Saad F, et al. ESMO 2022. Abstract #1357O

1L, first line; ABI, abiraterone; mCRPC; metastatic castration-resistant prostate cancer; OLA, Olaparib; PBO, placebo; PTS, patients

PROpel: BACKGROUND AND STUDY DESIGN

- **In the PROpel primary analysis, abiraterone + olaparib significantly prolonged radiographic progression-free survival (rPFS) vs placebo + abiraterone in first-line mCRPC (HR 0.66, 95% CI 0.54-0.81; p<0.0001).**[1] Patients were enrolled irrespective of HRRm status
- Additional biomarker subgroups results, and updated results are presented from latest data-cut



Latest data cut: 14 March 2022

[a]Full dose of Olaparib and/or abiraterone used, in combination with prednisone or prednisolone 5 mg bid. [b]HRRm, homologous recombination repair mutation, including 14 genes panel.

1L, first-line; ADT, androgen deprivation therapy; BICR, blinded independent central review; BID, twice daily; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group ; HR, hazard ratio; HRR, homologous recombination repair gene mutations; mCRPC, metastatic castration resistant prostate cancer; mCSPC, metastatic castration sensitive prostate cancer; NHA, novel hormonal agents; ORR, objective response rate; OS, overall survival; PFS2, time to second progression; PO, orally; QD, per day; rPFS, radiographic progression-free survival; TFST, time to first subsequent therapy or death; TTPP, time to pain progression

1. Saad F, et al. J Clin Oncol 40, 2022 (suppl 6; abstr 11) (ASCO GU 2022 oral presentation); 2. Saad F, et al. Ann Oncol. 2022;33 (suppl_7): S616-S652 (ESMO 2022, oral presentation)

PROpel: RESULTS

EFFICACY

rPFS (investigator assessment) by biomarker	BRCAm		Non-BRCAm	
	ABI + OLA (n=47)	ABI + PBO (n=38)	ABI + OLA (n=343)	ABI + PBO (n=350)
Events, n (%)	14 (29.8)	28 (73.7)	148 (43.1)	194 (55.4)
Median rPFS (months)	NR	8.4	24.1	19.0
HR (95% CI)	0.23 (0.12-0.43)		0.76 (0.61-0.94)	

	ABI + OLA (n=399)	ABI + PBO (n=397)
rPFS (investigator assessment)		
Events, n (%)	199 (49.9)	258 (65.0)
Median rPFS (months)	25.0	16.4
HR (95% CI)	0.67 (0.56-0.81), p<0.0001	
OS		
Events, n (%)	107 (26.8)	121 (30.5)
Median OS (months)	NR	NR
HR (95% CI)	0.86 (0.66-1.12), p=0.29	

SAFETY

- Updated overall safety results from latest cut-off were consistent with the primary analysis
  - One case of MDS/AML identified during hospital admission for COVID-19 pneumonia
  - Incidence of primary malignancies and pneumonitis balanced between arms
  - Incidence of pulmonary embolism and cardiovascular events similar between primary analysis and latest data cut

ABI, abiraterone; AML, acute myeloid leukaemia; BRCAm, BRCA mutation carrier ; CI, confidence interval; HR, hazard ratio; MDS, myelodysplastic syndrome; NR, not reached; rPFS, radiographic progression-free survival; OLA, Olaparib; OS, overall survival; PBO, placebo

Saad F, et al. Ann Oncol. 2022;33 (suppl_7): S616-S652 (ESMO 2022, oral presentation)

PROpel: SUMMARY

- Meaningful rPFS improvement of ≥5 months was observed with ABI + OLA vs ABI + PBO in all assessed biomarker subgroups in 1L mCRPC patients
  - The rPFS effect was most pronounced in the BRCAm subgroup
- Updated results show a continuing trend towards improved OS and support a superior clinical benefit with ABI + OLA vs ABI + PBO as 1L therapy for pts with mCRPC
- Safety and tolerability results were consistent with the primary analysis and the known safety profiles for abiraterone and olaparib

Clinical Perspective

- **PARP inhibition still requires molecular stratification**

1L, first line; BRCAm, BRCA mutation carrier; mCRPC; metastatic castration resistant prostate cancer; OS, overall survival; PARP, Poly (ADP-ribose) polymerase; rPFS, radiographic progression-free survival

Saad F, et al. Ann Oncol. 2022;33 (suppl_7): S616-S652 (ESMO 2022, oral presentation); de Bono J. Discussant of abstract # 1357O, ESMO 2022.

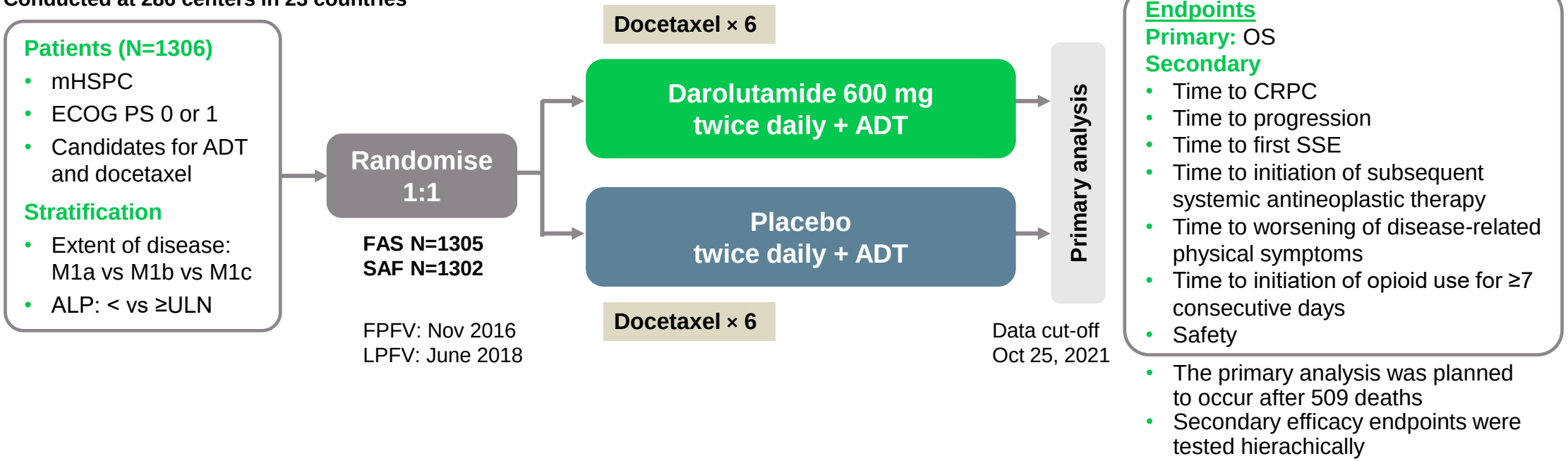
QUALITY OF LIFE AND PATIENT-RELEVANT ENDPOINTS WITH DAROLUTAMIDE IN THE PHASE 3 ARASENS STUDY

Fizazi K, et al. ESMO 2022. Abstract #1360MO

ARASENS: BACKGROUND AND STUDY DESIGN

- In ARASENS, darolutamide + ADT + docetaxel significantly reduced risk of death by 32.5% vs placebo + ADT + docetaxel in patients with mHSPC
- QOL and patient-relevant endpoints are reported here

Randomised, double-blind, placebo-controlled, global, phase 3 study (NCT02799602)
Conducted at 286 centers in 23 countries



ADT, androgen deprivation therapy; ALP, alkaline phosphatase; CRPC, castration-resistant prostate cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; FAS, full analysis set; FPFV, first patient first visit; LPFV, last patient first visit; M1a, nonregional lymph node metastases; M1b, bone metastases +/- lymph node metastases; M1c, visceral metastases +/- lymph node or bone metastases; mHSPC, metastatic hormone sensitive prostate cancer; OS, overall survival; QOL, quality of life; SAF, safety analysis set; SSE, symptomatic skeletal event; ULN, upper limit of normal

Fizazi K, et al. Ann Oncol. 2022;33 (suppl_7): S616-S652 (ESMO 2022, oral presentation)

ARASENS: RESULTS

EFFICACY

- Most patients had high baseline QoL scores and had no pain or only mild pain at baseline (81%)

		Median time (mo) to deterioration (95% CI)		
	QoL and Pain measures	Daro + ADT + Doce	PBO + ADT + Doce	HR (95% CI)
Overall population	NCCN-FACT-FPSI17 DRS-physical	19.3 (13.8-24.8)	19.4 (15.4-27.6)	1.04 (0.89-1.22)
	BPI-SF pain interference	NE (NE-NE)	NE (NE-NE)	0.86 (0.64-1.15)
Pts with moderate or severe baseline pain	NCCN-FACT-FPSI17 DRS-physical	NE (NE-NE)	41.4 (36.1-NE)	0.63 (0.39-1.04)
	BPI-SF pain interference	NE (NE-NE)	NE (NE-NE)	0.60 (0.29-1.24)

SAFETY

- The cumulative incidence of most AEs of special interest were generally low and similar across both arms after median follow up of >3.5 years

	Cummulative incidence (%)		
	Daro + ADT + Doce	PBO + ADT + Doce	HR (95% CI)
Time to fall	6.6	4.6	1.05 (0.65-1.69)
Time to fatigue	33.1	32.9	0.95 (0.79-1.15)
Time to fracture	7.5	5.1	1.09 (0.70-1.70)
Time to mental impairment disorder	3.5	2.3	1.16 (0.60-2.25)
Time to rash	16.6	13.5	1.15 (0.87-1.53)
Time to cardiac disorder	10.9	11.7	0.76 (0.54-1.05)
Time to hypertension	13.7	9.2	1.20 (0.86-1.67)

ADT, androgen deprivation therapy; AE, adverse event; BPI-SF, Brief Pain Inventory - Short Form; CI, confidence interval; Daro, darolutamide; Doce, docetaxel; DRS, disease-related symptoms; HR, hazard ratio; mo, months; NCCN-FACT-FPSI17, National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy Prostate Cancer Symptom Index 17-item questionnaire; NE, not estimable; PBO, placebo; pts, patients; QOL, quality of life

Fizazi K, et al. Ann Oncol. 2022;33 (suppl_7): S616-S652 (ESMO 2022, oral presentation)

ARASENS: SUMMARY

- Early treatment intensification with darolutamide + ADT + docetaxel improved patient-relevant endpoints vs placebo + ADT + docetaxel
  - including a reduction in all-cause and prostate cancer related deaths
- Quality of life was maintained over time, and darolutamide had no adverse impact on quality of life, including in patients with poor prognosis
  - Similar incidences and time course for most adverse events of special interest, notably with no increase in cardiac disorders

Clinical Perspective

- **Darolutamide in combination with ADT and docetaxel sets a new standard of care for treatment of mHSPC**

ADT, androgen deprivation therapy; Daro, darolutamide; mHSPC, metastatic hormone sensitive prostate cancer

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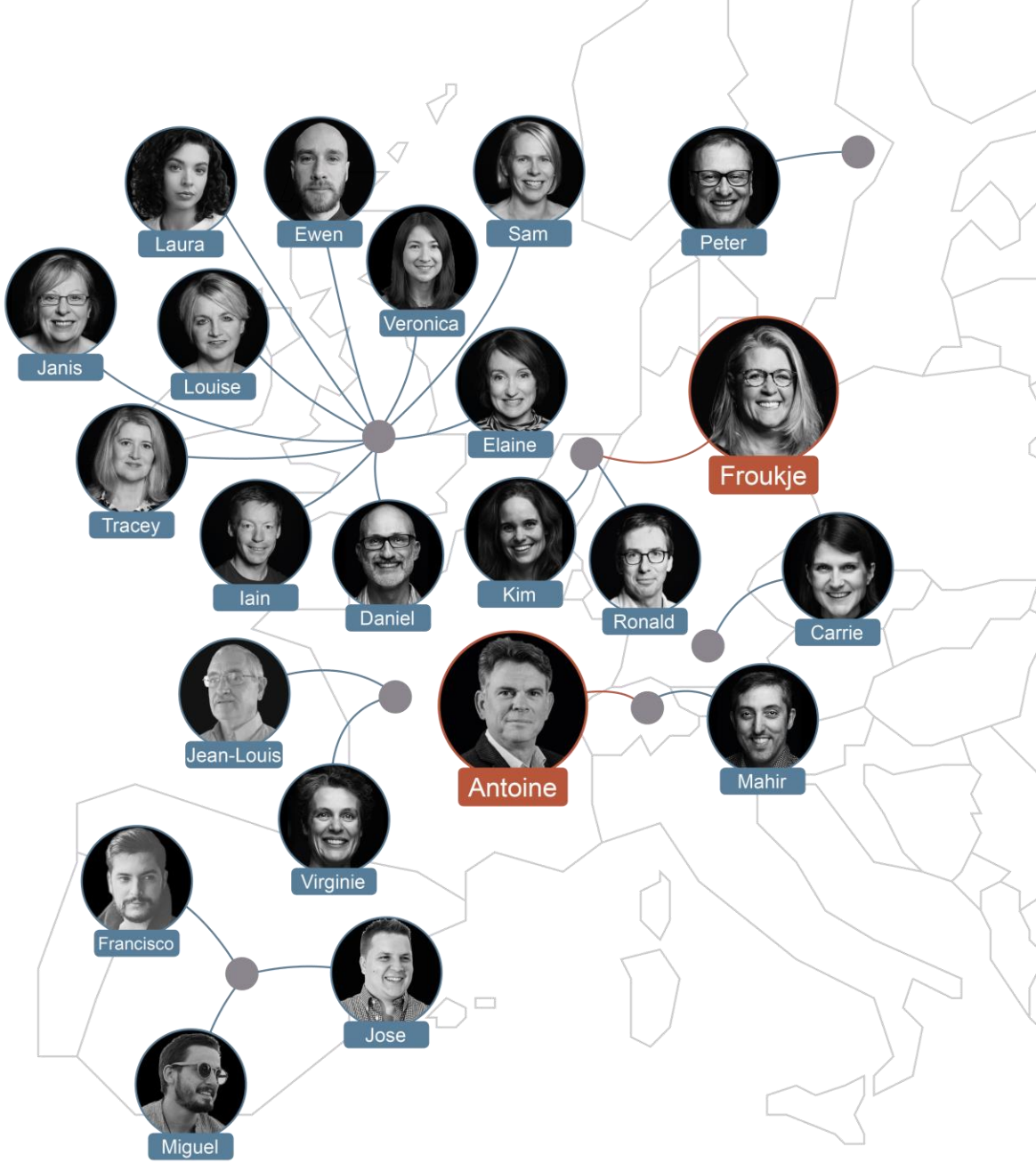

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