ACONTECEU NO EAU 2024

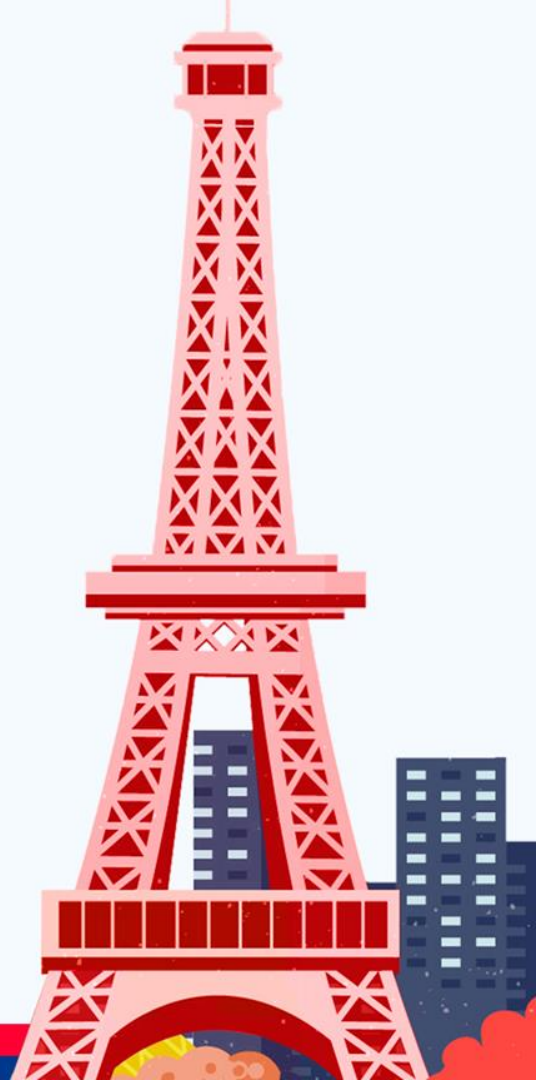
Apresentado por: Breno Dauster

SOCIEDADE BRASILEIRA DE UROLOGIA

São Paulo

Apoio: Janssen Oncology

PHARMACEUTICAL COMPANIES OF Johnson&Johnson



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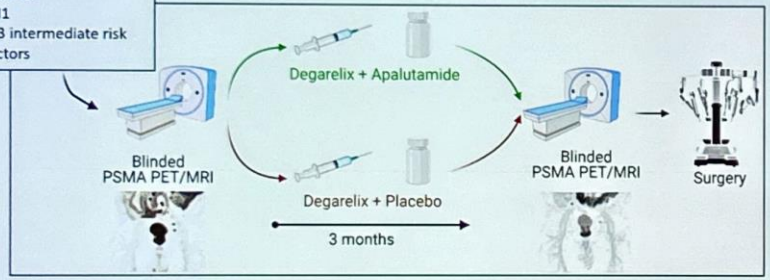
Devos G et al. European Urology, 2023

ARNEO trial

A double-blind, placebo controlled randomized phase II trial of neoadjuvant degarelix with or without apalutamide prior to radical prostatectomy for high-risk prostate cancer

High-risk PCa, M0:
- cT3-4
- PSA>20
- GS 8-10
- cN1
- 2-3 intermediate risk factors



Primary endpoint:
Difference in % Minimal Residual Disease (<0.25ml)

Secondary endpoints:
- Tumor downstaging, PSA kinetics, toxicity, QoL, biomakers for pathological response
- BCR-free survival at 3 years follow-up

- All patients were followed-up 3-monthly until PSA >0.2 ng/ml
- No patient received adjuvant RT or ADT
- At PSA >0.2 ng/ml, patients received a PSMA PET/CT

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Variable	Degarelix + placebo (*n* = 44)	Degarelix + apalutamide (*n* = 45)
Age at time of inclusion (yr), median (IQR)	67 (62–70)	66 (61–70)
ECOG performance status		
0	42 (96)	41 (91)
1	2 (4)	4 (9)
Race		
White	43 (98)	45 (100)
Black	1 (2)	0
PSA at time of biopsy (ng/ml), median (IQR)	11.2 (8.1–19.3)	12.6 (7.8–19.7)
<10 (%)	20 (45)	20 (44)
10–20 (%)	14 (32)	14 (31)
>20 (%)	10 (23)	11 (25)
Clinical T stage (MRI based)		
cT1	1 (2)	1 (2)
cT2	11 (25)	11 (24)
cT3a	20 (46)	18 (40)
cT3b	7 (16)	12 (27)
cT4	5 (11)	3 (7)
Clinical T stage (DRE based)		
cT1	12 (27)	11 (25)
cT2	11 (25)	19 (42)
cT3	20 (46)	13 (29)
NA	1 (2)	2 (4)
Clinical N stage (cross-sectional imaging CT and/or MRI)		
cN1	5 (11)	7 (16)
Biopsy method		
Targeted	13 (30)	13 (29)
Targeted + systematic	22 (50)	25 (55)
Systematic	9 (20)	7 (16)
Biopsy Gleason score		
3 + 4 = 7 (ISUP 2)	3 (7)	5 (11)
4 + 3 = 7 (ISUP 3)	10 (23)	11 (24)
8 (ISUP 4)	17 (39)	10 (22)
9–10 (ISUP 5)	14 (32)	19 (42)
Positive biopsies involved (%), median (IQR)[a]	46 (37–56)	45 (35–67)
Intraductal growth at biopsy		
Yes	10 (23)	6 (13)
Cribriform pattern at biopsy		
Yes	33 (75)	26 (58)
Risk group		
High risk	43 (98)	44 (98)
Intermediate risk	1 (2)	1 (2)

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Table 3 – PSA, testosterone, and SHBG kinetics

Variable	Degarelix + placebo (n = 44)	Degarelix + apalutamide (n = 45)
PSA at study entry, median (IQR)	13 (9.7–20)	13 (7.9–22)
PSA kinetics during neoadjuvant treatment (ng/ml), median (IQR)		
End of cycle 1	3.2 (2.2–4.3)	1.2 (0.72–1.8)
End of cycle 2	1.7 (0.87–2.6)	0.28 (0.18–0.41)
End of cycle 3	1.2 (0.64–2.4)	0.11 (0.050–0.19)
PSA nadir before RP <0.3 ng/ml	4 (9.1)	39 (87)
Detectable PSA (ng/ml) at 6 wk after RP (%)	3 (7)	2 (4)
Testosterone at study entry (ng/dl), median (IQR)	430 (325–490)	363 (272–493)
Testosterone at end of cycle 3 (ng/dl), median (IQR)	10 (7.7–14)	12 (8.1–15)
Testosterone at 6 wk after RP (ng/dl), median (IQR)	11 (0–22)	7.7 (0–16)
SHBG at study entry, median (IQR)	42 (34–56)	40 (32–60)
SHBG following neoadjuvant treatment, median (IQR)	48 (35–60)	93 (71–121)

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Conclusões do ARNEO – EAU2022

• Pacientes tratados com degarelix + Apa atingiram uma melhor resposta patológica tumoral que os tratados com Degarelix + Placebo

➢ MRD (< 0.25 mL) 38% APA arm versus 9% Placebo arm (p = 0.002), Volume doença Residual APA vs 1.7 mL Placebo (p < 0.001):

• Volume doença estimado com PSMA PET/CT e SUVmax PSMA PET após neoadjuvância prediz resposta atológica

➢ Downstaging mais frequente APA (51% vs 27%, p = 0.03)

• Perda de expressão do PTEN é um preditor negativo para DRM

➢ PTEN loss reduziu chance de atingir DRM (11% versus 43%, p = 0.002).

• Esses resultados oferecem uma base sólida para estudos Fase 3

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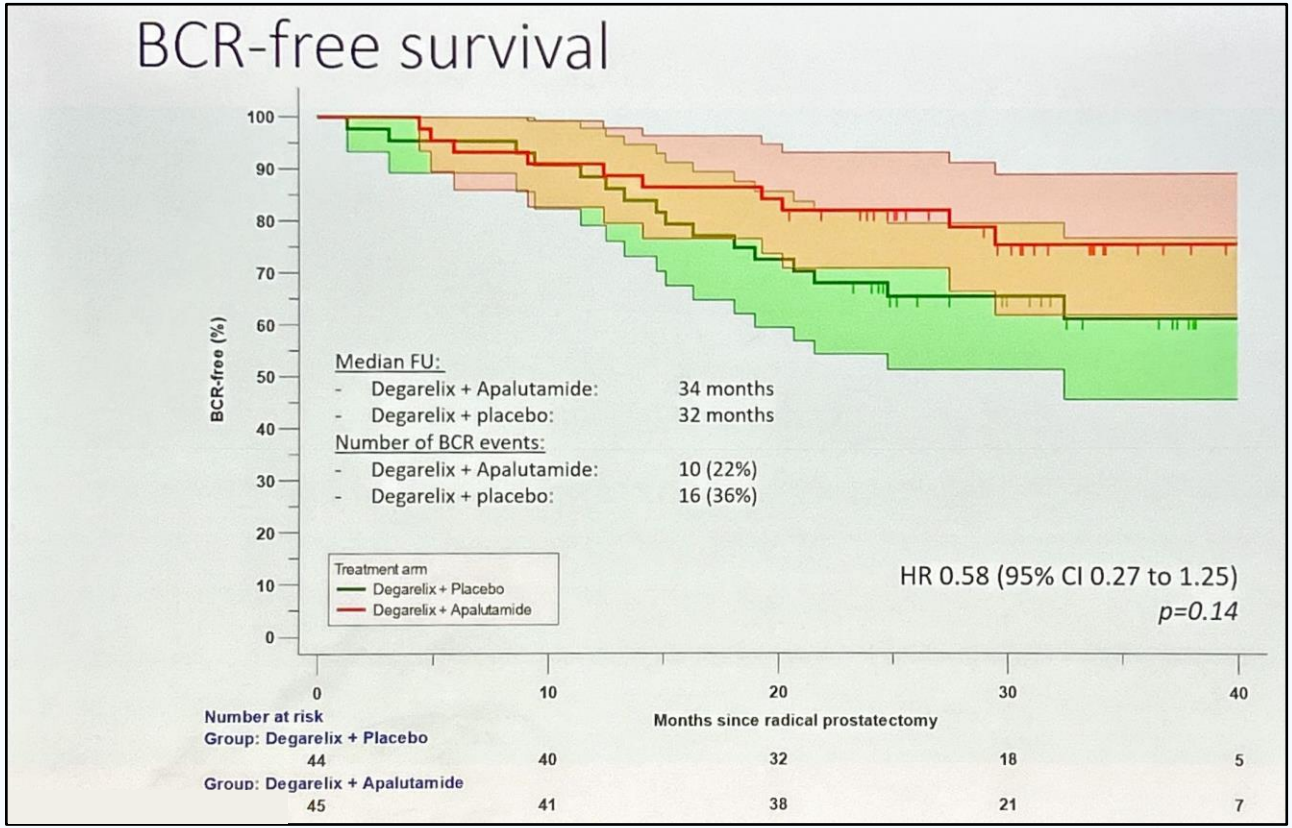

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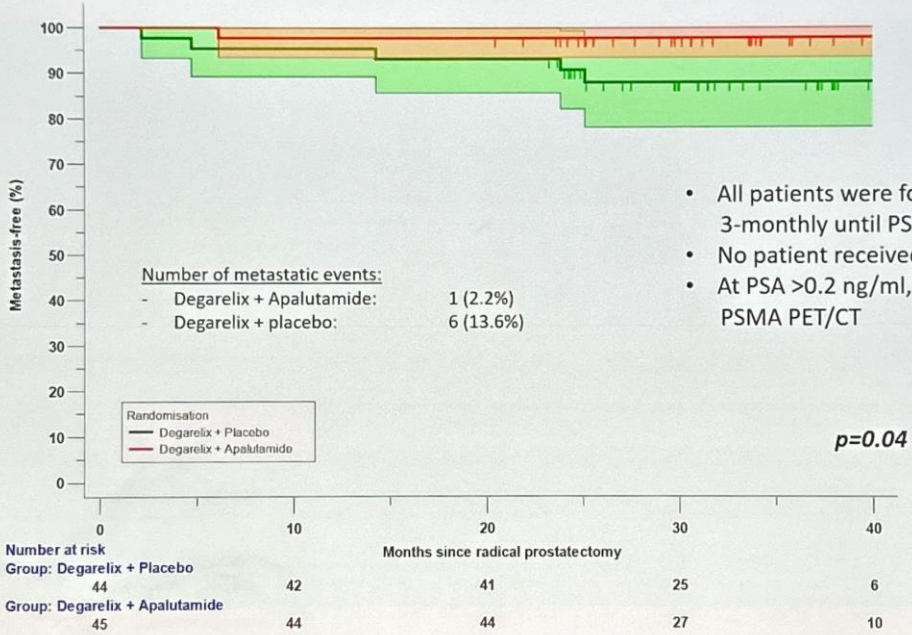
Metastasis-free survival



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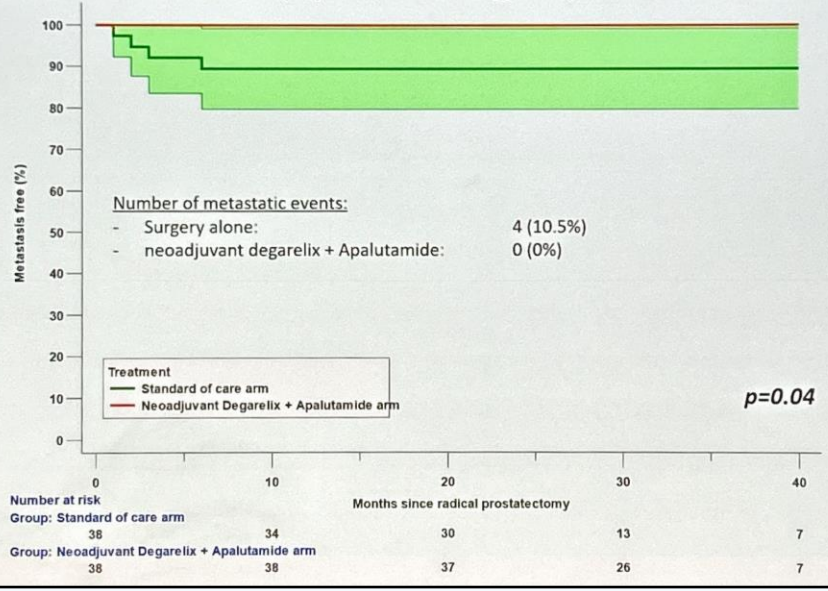
Metastasis-free survival: intense neoadjuvant hormonal therapy vs. Surgery alone (matched cohort)



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Conclusions

- At 3 year follow-up, there is a trend towards improved BCR-free and metastasis-free survival with neo-adjuvant treatment intensification.
- Patients treated with neoadjuvant ADT + apalutamide had improved metastatic disease-free survival against the standard of care (surgery alone) in a matched cohort.