



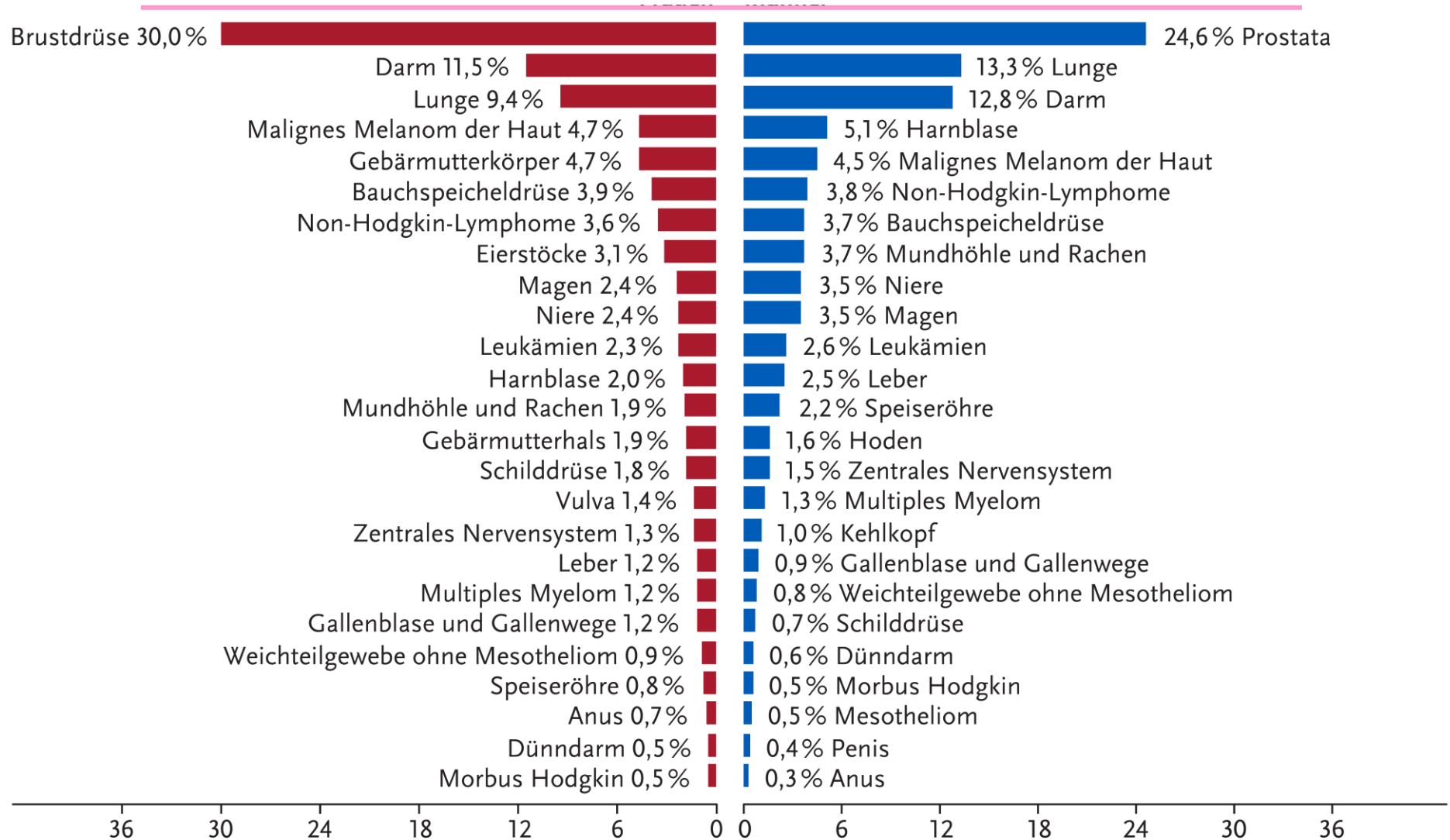
Das metastasierte Prostatakarzinom

hormonsensitiv

14. Oktober 2023

Krebs in Deutschland

Verteilung



Prostatakarzinom

Metastasierung



Gehirn

Leber

Lymphknoten

**Der Patient hat meistens Recht.
Knochen**

Prostatakrebs

Diagnostik bei Verdacht auf Metastasen

Krankengeschichte, körperliche Untersuchung

Labor

PSA

AP, Ca, Blutbild, Nierenwerte

Bildgebung

CT

hohe Genauigkeit, auch Knochen

MRT

Weichteile

Knochenszintigraphie

alle Knochen, keine Größenmessung

PET (CT, MRT)

aktive Herde

Prostatakrebs

Diagnostik bei Verdacht auf Metastasen

Krankengeschichte, körperliche Untersuchung

Labor

PSA

AP, Ca, Blutbild, Nierenwerte

Bildgebung

CT

MRT

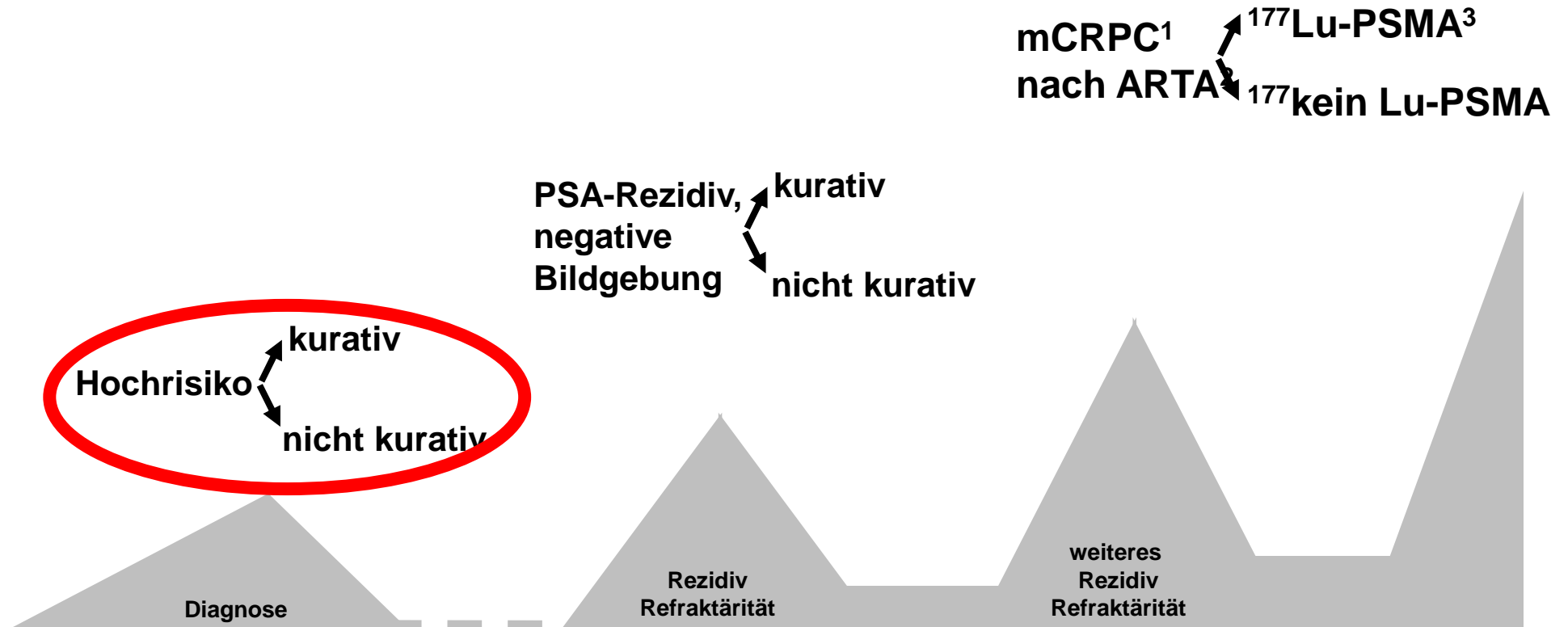
Knochenszintigraphie

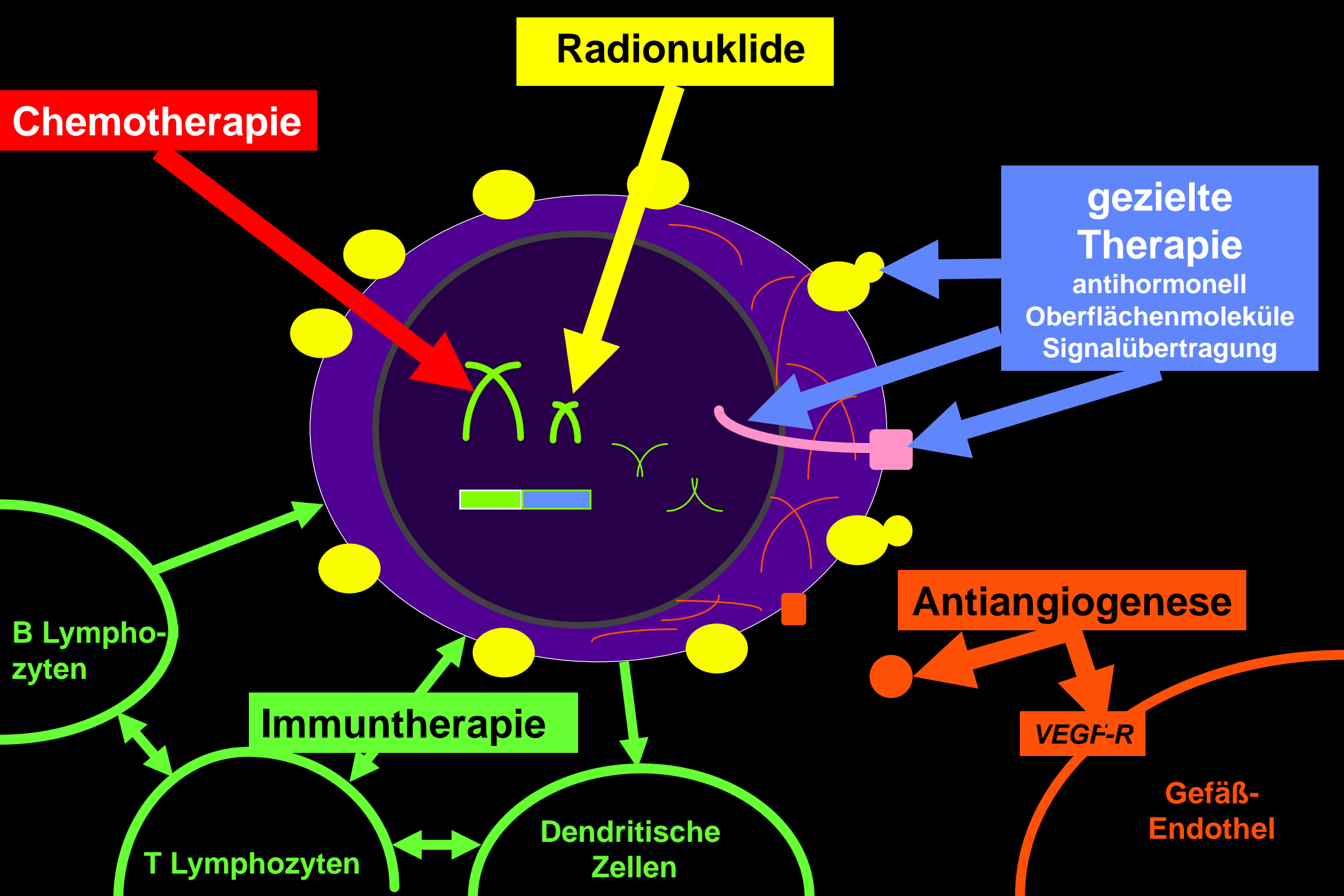
PET

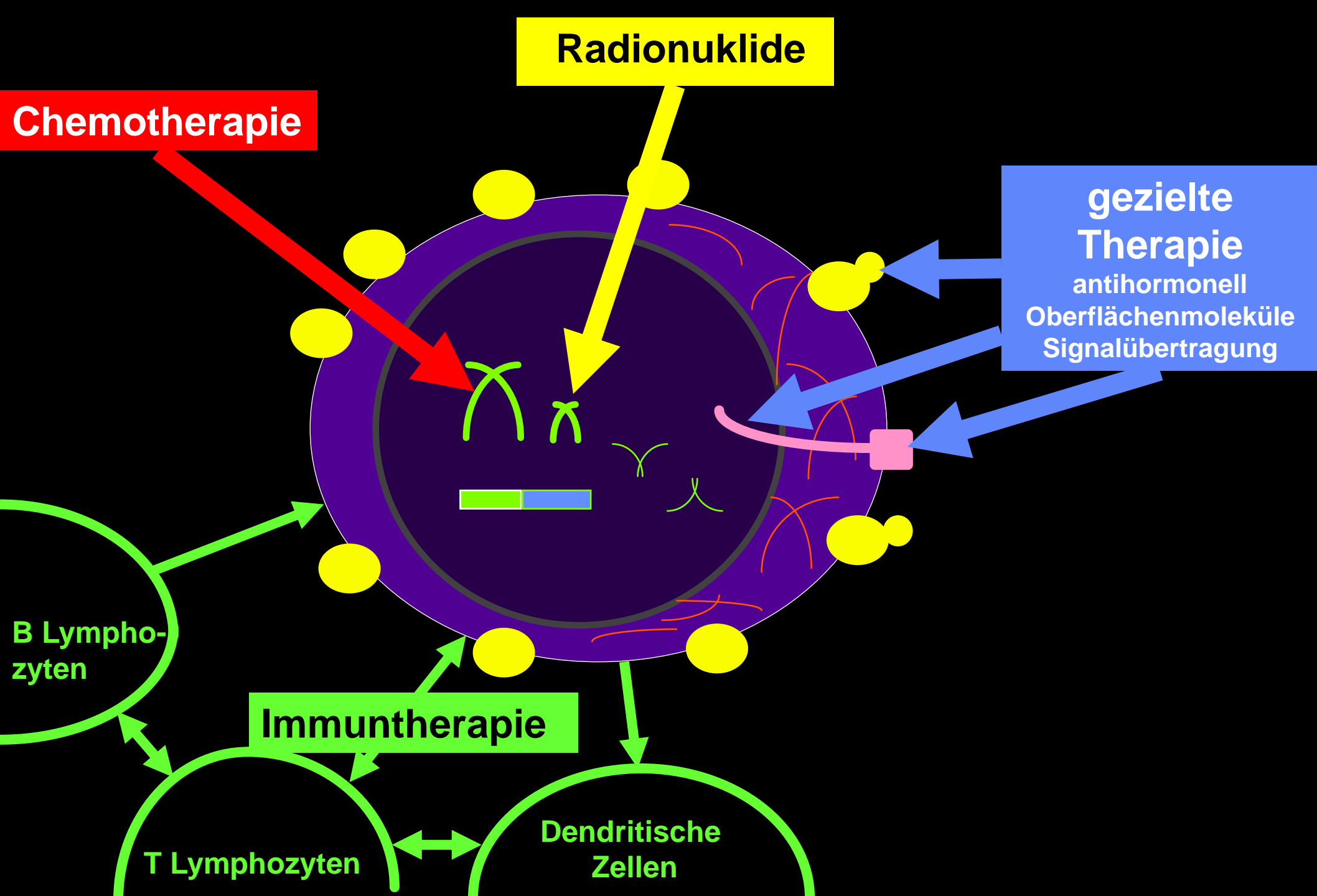


Prostatakrebs

PET - Indikationen







Radionuklide

Chemotherapie

gezielte Therapie
antihormonell
Oberflächenmoleküle
Signalübertragung

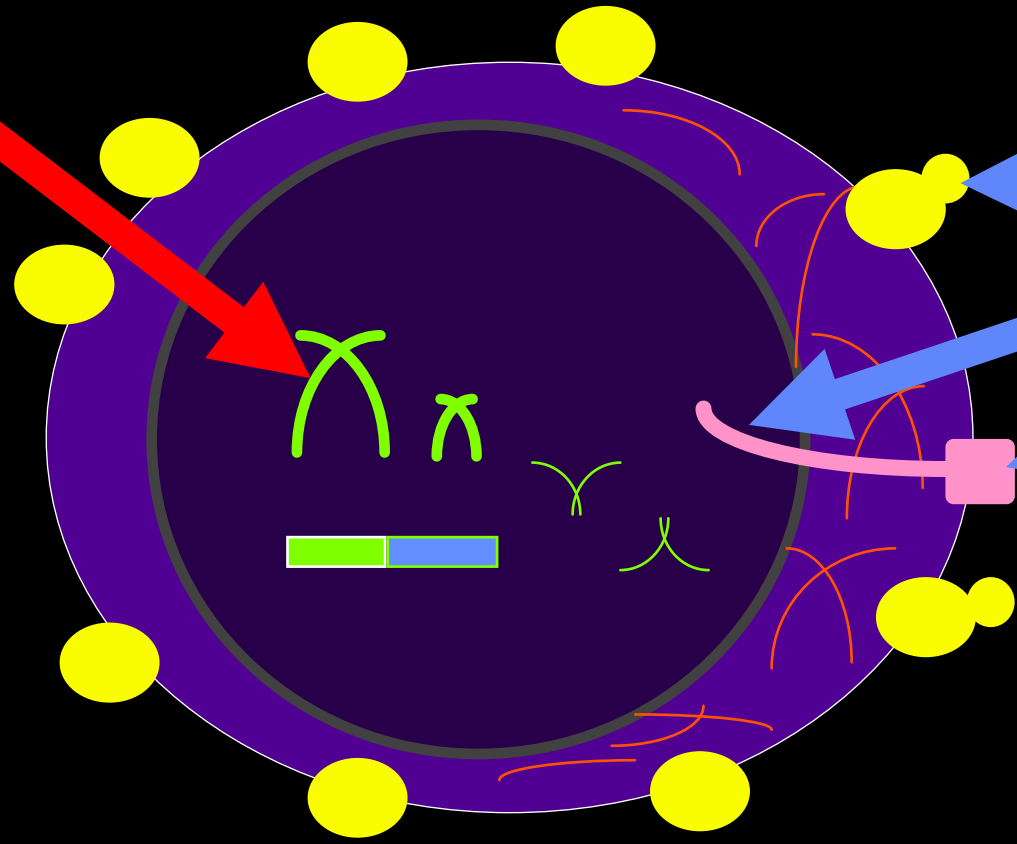
B Lymphozyten

Immuntherapie

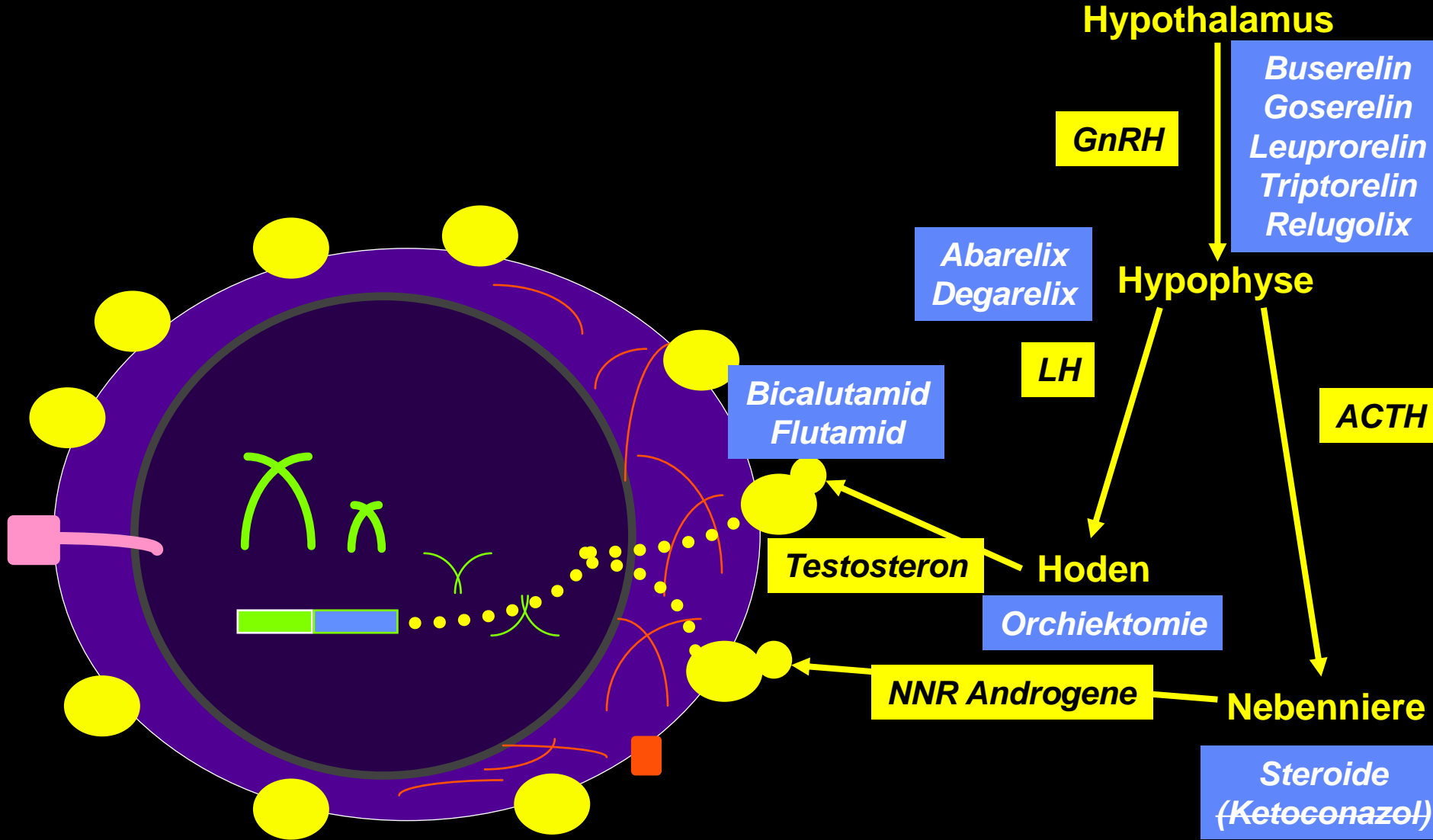
T Lymphozyten

Dendritische Zellen

Chemotherapie



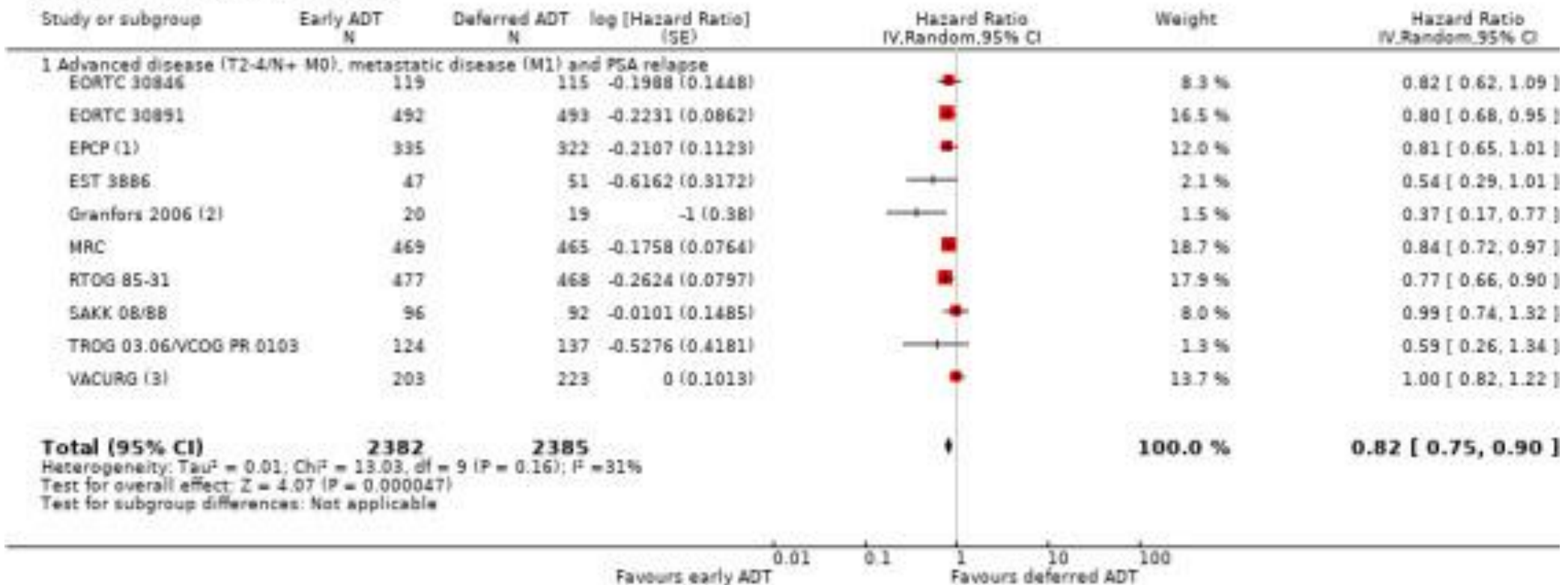
**gezielte
Therapie**
antihormonell
Oberflächenmoleküle
Signalübertragung



Prostatakrebs

ADT – früh vs verzögert

Review: Early versus deferred standard androgen suppression therapy for advanced hormone-sensitive prostate cancer
 Comparison: 1 Early vs deferred ADT
 Outcome: 1 Time to death of any cause



(1) only participants included with locally advanced disease receiving bicalutamide/placebo in combination with watchful waiting

(2) only participants with lymph-node positive disease were included

(3) only patients with metastatic disease (M1) treated with orchiectomy+placebo vs placebo were included

Prostatakarzinom

Androgendeprivation – Zusammenfassung

Erektile Dysfunktion

Phosphodiesterasehemmer

Hitzewallungen

Medikamente

Gynäkomastie

Bestrahlung, (Tamoxifen)

Muskelabbau

körperliche Aktivität

Anämie

Eisen? ESA?

Reduktion der Knochendichte

Vit. D + Calcium,

körperliche Aktivität

Bisphosphonate, Denosumab

Metabolisches Syndrom

körperliche Aktivität

Kontrolle

Medikamente

Fatigue

?, geistige Aktivität, Gehirnjogging



Tabelle 2: Relugolix beim fortgeschrittenen Prostatakarzinom

Erstau- tor / Jahr	Studie	Risikogruppe	Kontrolle	Neue The- rapie	N ¹	PSA-An- sprechrte ²	Schwere kar- diovaskuläre Ereignisse ³ (HR ⁴)	ÜL ⁵ (HR ⁴)
Shore, 2020 [11], Dossier	HERO	fortgeschritten	Leuprorelin	Relugolix	1074 (2:1)	22,7 vs 79,8 ⁶ p < 0,0001	5,9 vs 3,2 ⁶ 0,539 ⁷ p = 0,0405	n. e. vs n. e. ⁹ 0,363 n. s.
Dossier	HERO	fortgeschritten, für lokale Thera- pie nicht geeig- net	Leuprorelin	Relugolix	640 (2:1)	14,6 vs 77,5 ⁶ p < 0,0001	5,2 vs 1,2 ⁶ 0,223 ⁷ p = 0,0054	n. e. vs n. e. ⁹ 0,692 n. s.

¹ N - Anzahl Pat.; ² PSA Ansprechrate: Reduktion des initialen PSA-Wertes um >50% in Woche 3 Tag1 und bestätigt in Woche 5

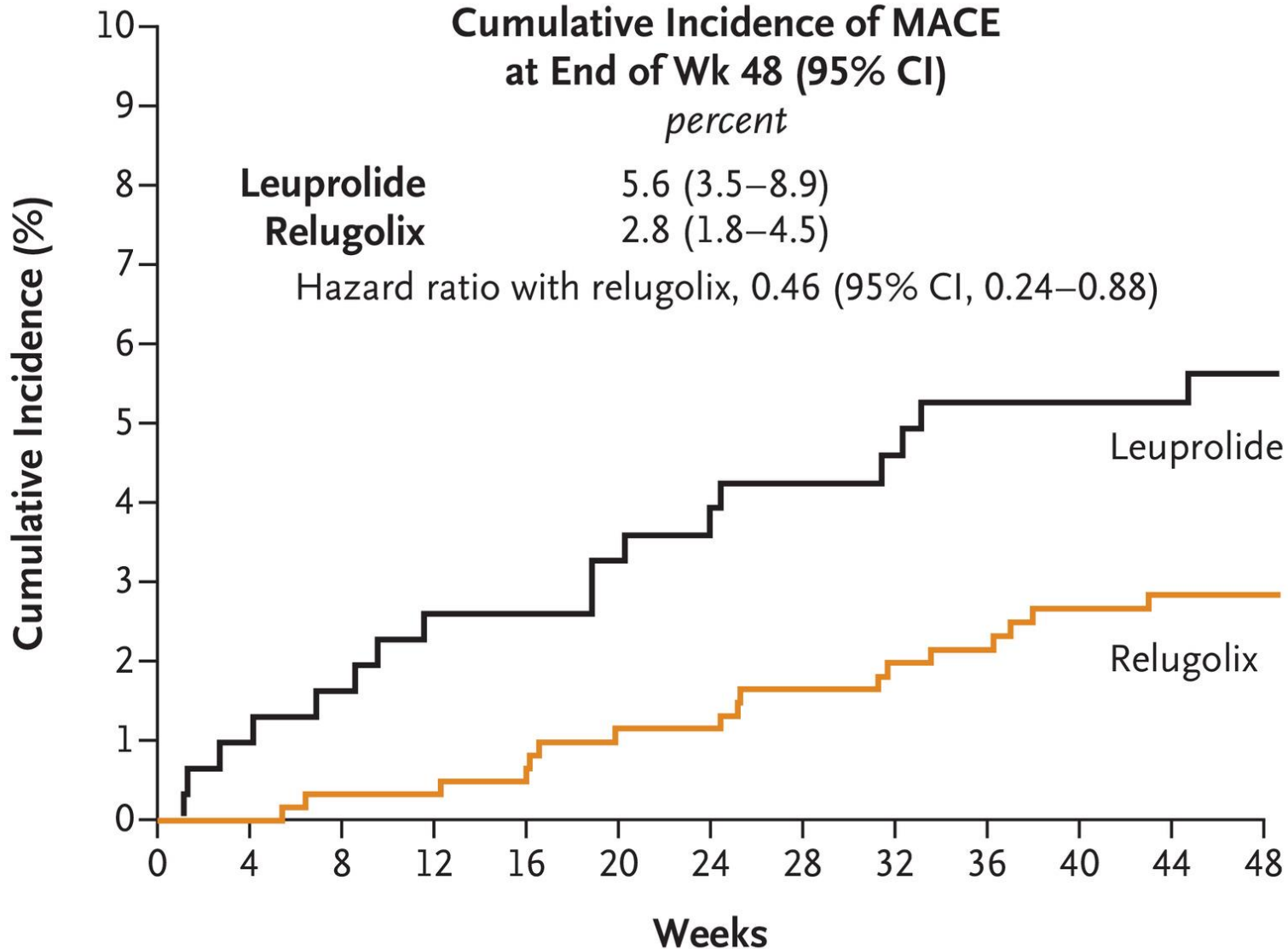
Cumulative Incidence of MACE at End of Wk 48 (95% CI)

percent

Leuprolide 5.6 (3.5–8.9)

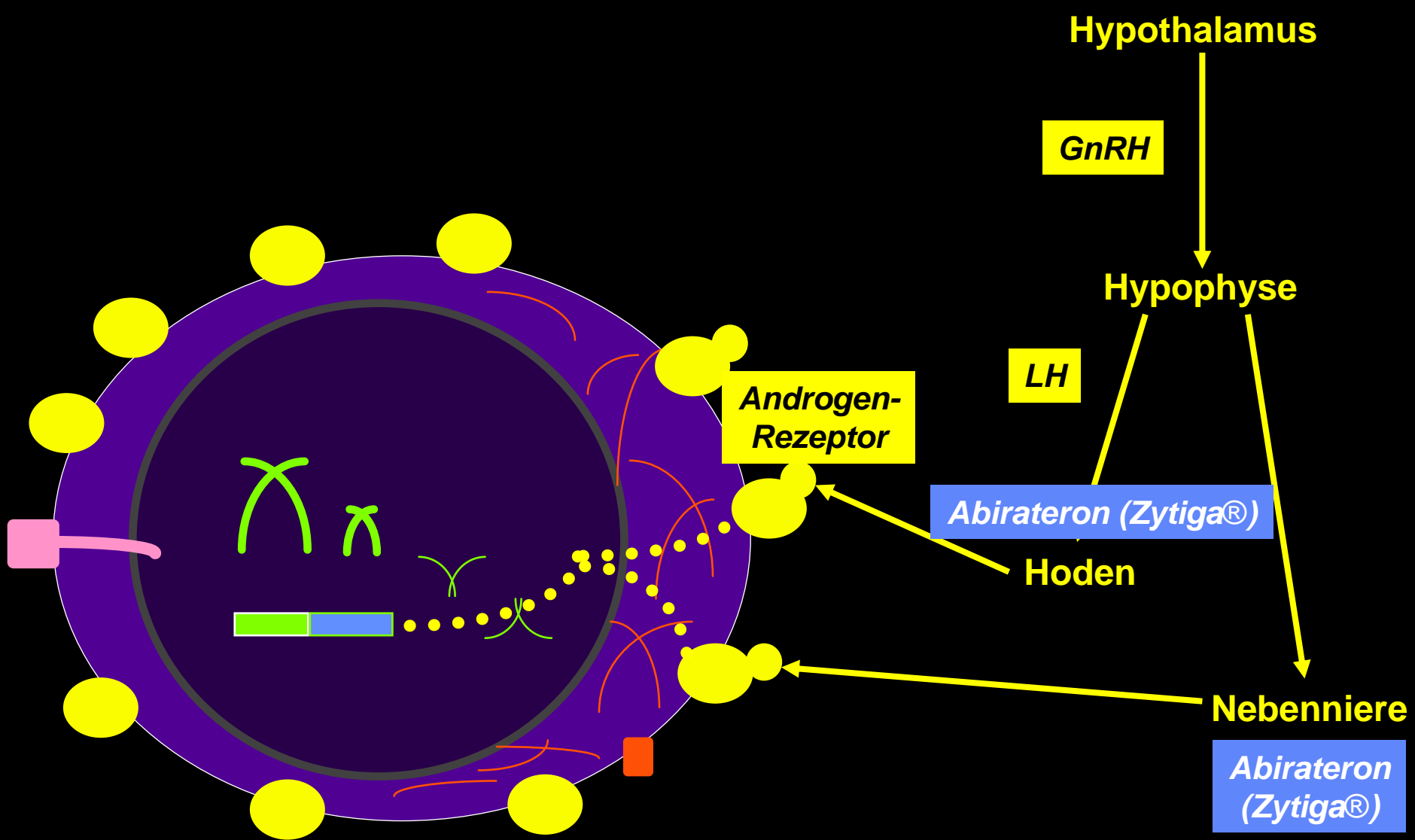
Relugolix 2.8 (1.8–4.5)

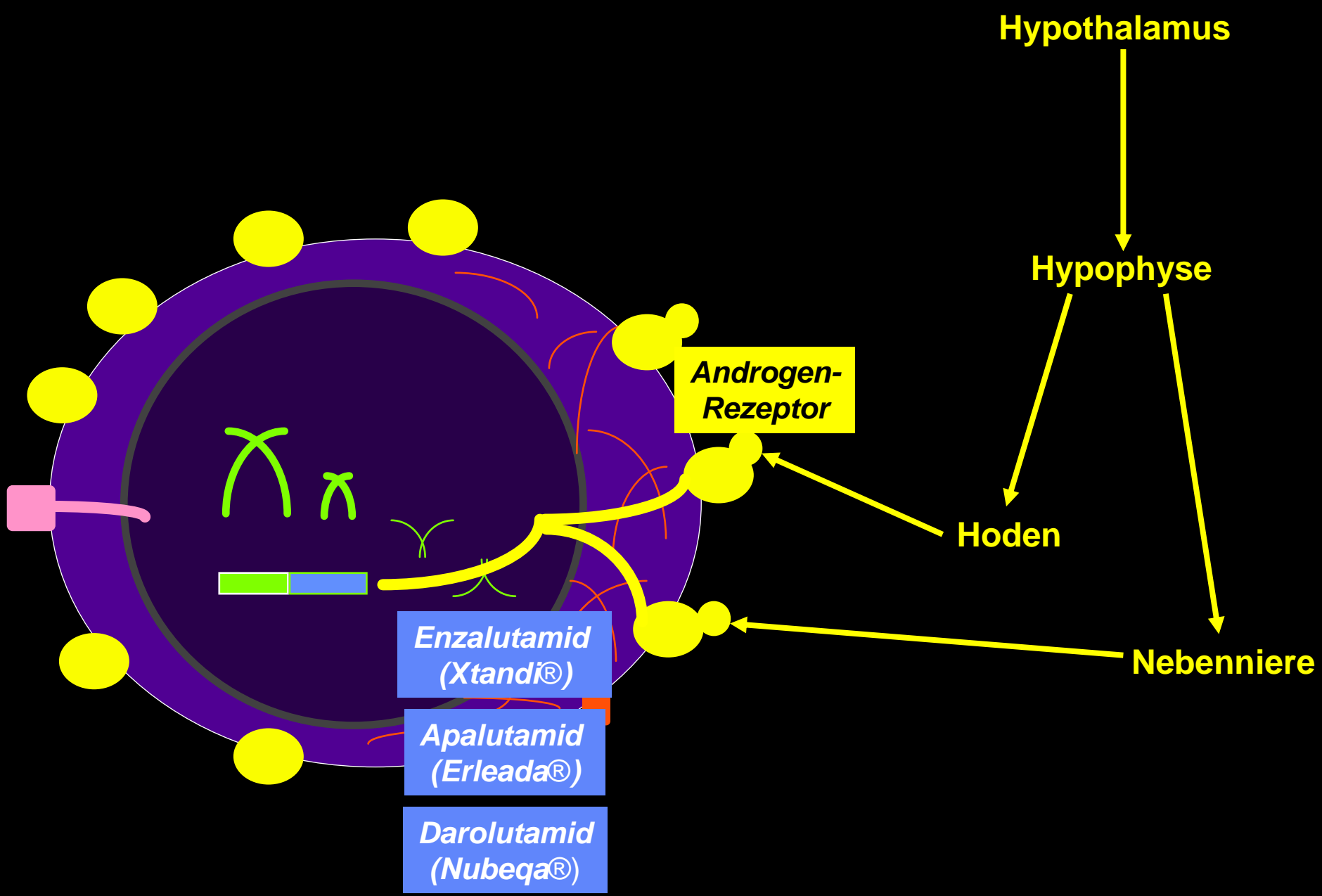
Hazard ratio with relugolix, 0.46 (95% CI, 0.24–0.88)



No. at Risk

Leuprolide	308	305	303	298	298	293	292	288	281	279	278	269	259
Relugolix	622	621	616	610	605	596	595	588	582	575	563	559	538

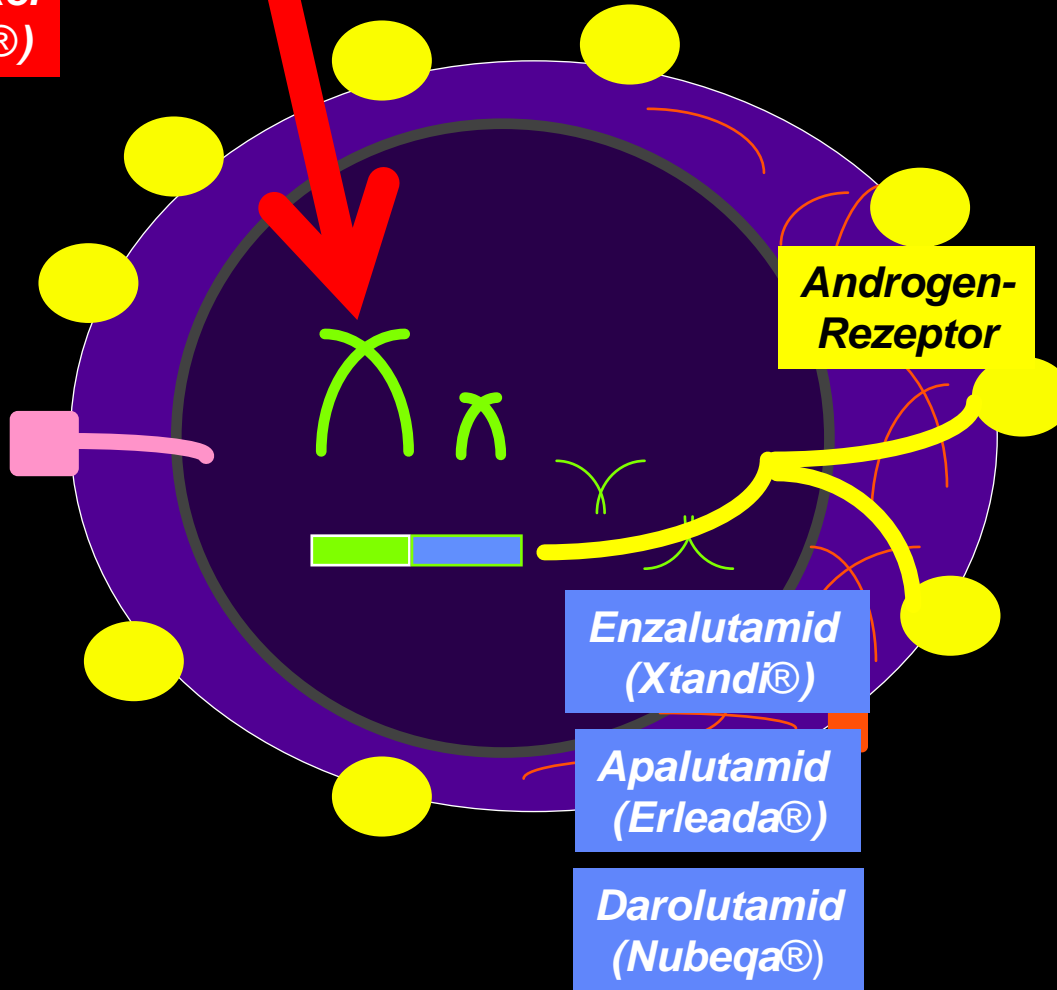




Chemotherapie

Docetaxel

Cabazitaxel
(*Jevtana*®)

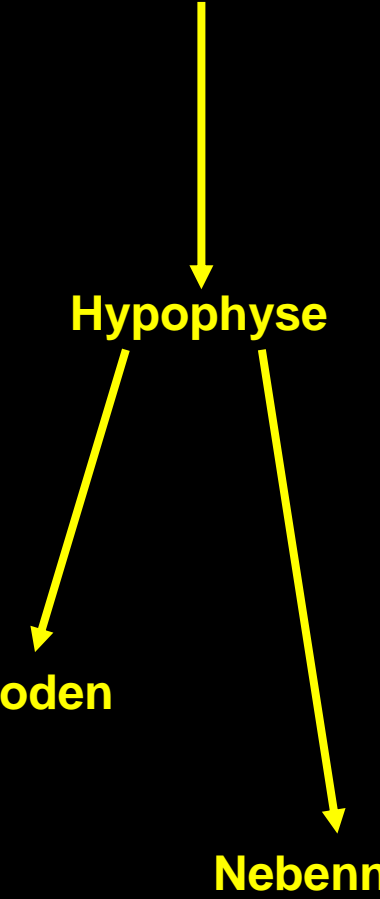


Hypothalamus

Hypophyse

Hoden

Nebenniere



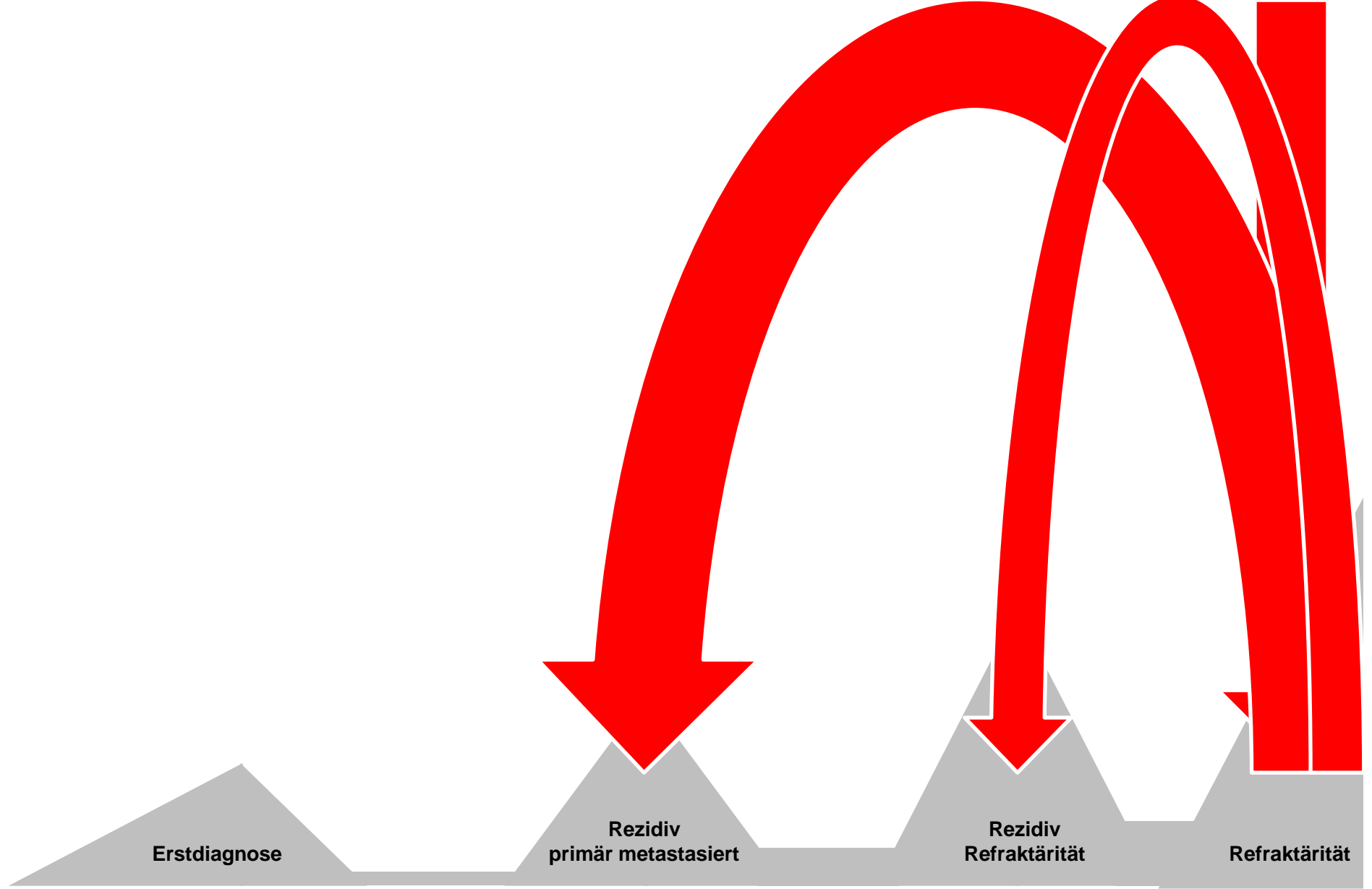


TABLE 1. Summary Data of Completed Trials in Metastatic Hormone-Sensitive Prostate Cancer**Doublet Systemic Therapy**

Trial	Patients Enrolled	Intervention Arm	Control Arm	Previous/ Concurrent Docetaxel	Median Follow-Up (months)	Median OS in Intervention Arm (months)	Median OS in Control Arm (months)	Group: HR (95% CI)	P
CHAARTED ⁷	790	ADT plus docetaxel	ADT	Not allowed	53.7	57.6	47.2	0.72 (0.59 to 0.89)	.0018
STAMPEDE (M1 subgroup) ⁸	1,086	ADT plus docetaxel	ADT	Not allowed	78.2	59.1	43.1	0.81 (0.69 to 0.95)	.003
LATITUDE ¹⁰	1,199	ADT plus abiraterone plus prednisone	ADT plus placebo	Not allowed	51.8	53.3	36.5	0.66 (0.56 to 0.78)	<.0001
STAMPEDE ⁹	1,917	ADT plus abiraterone plus prednisone	ADT	Not allowed	40	NR	NR	Overall: 0.63 (0.52 to 0.76) M1 subgroup: 0.61 (0.49 to 0.75)	<.001 (overall)
ENZAMET ¹⁶	1,125	ADT plus enzalutamide	ADT plus NSAA	Allowed (concurrent, 45%)	68	NR	NR	Overall: 0.70 (0.58 to 0.84) Early docetaxel: 0.82 (0.63 to 1.06) No early docetaxel: 0.60 (0.47 to 0.78)	<.0001 (overall)
ARCHES ¹¹	1,150	ADT plus enzalutamide	ADT plus placebo	Allowed (previous, 18%)	44.6	NR	NR	Overall: 0.66 (0.53 to 0.81) Previous docetaxel: 0.74 (0.46 to 1.20) No previous docetaxel: 0.64 (0.51 to 0.81)	<.001 (overall)
TITAN ¹²	1,052	ADT plus apalutamide	ADT plus placebo	Allowed (previous, 11%)	44	NR	52.2	Overall: 0.65 (0.53 to 0.79) Previous docetaxel: 1.12 (0.59 to 2.12) No previous docetaxel: 0.61 (0.50 to 0.76)	<.0001 (overall)

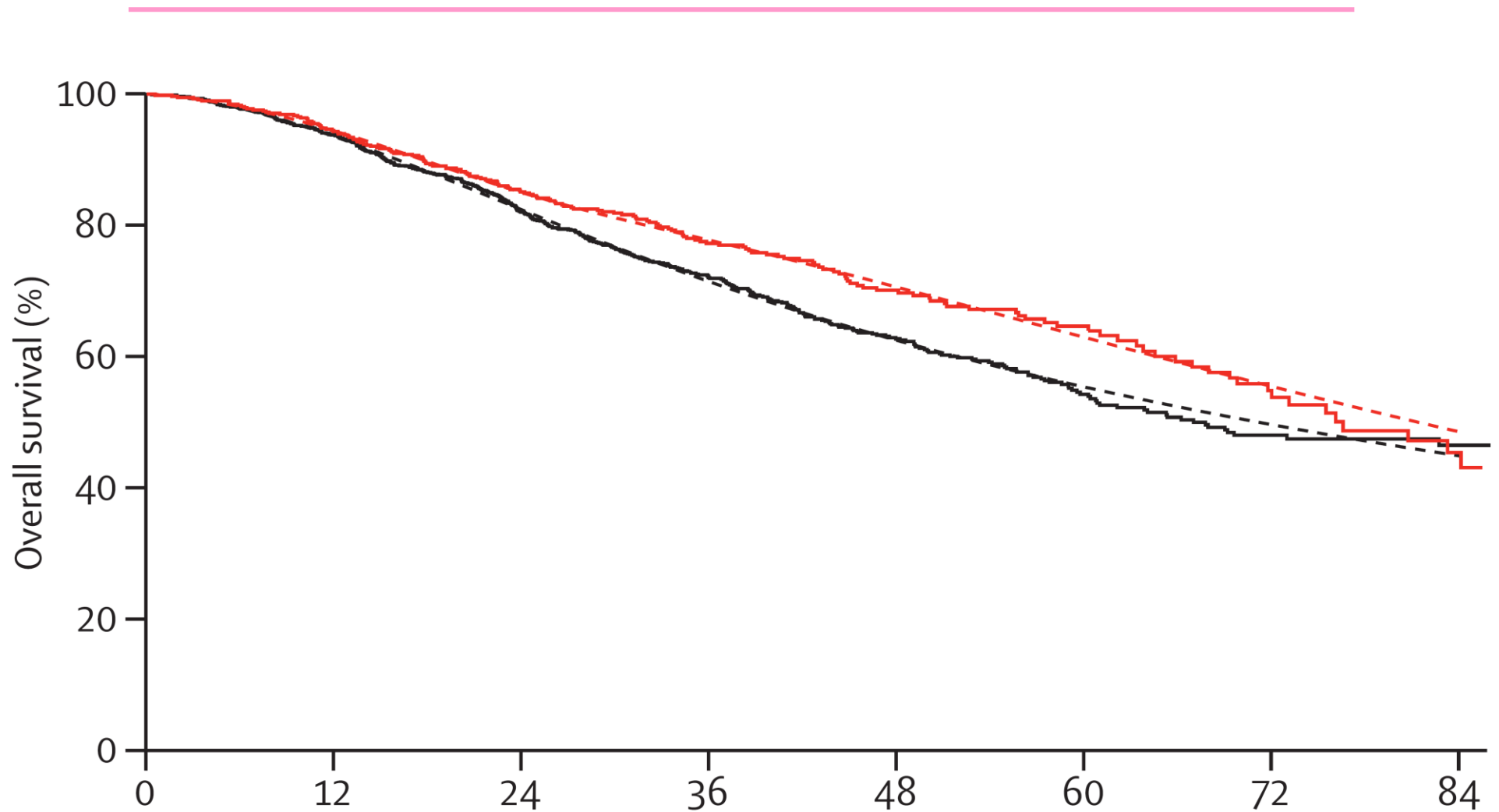
Triplet Systemic Therapy

Trial	Patients Enrolled	Intervention Arm	Control Arm	% Synchronous	% High-Volume	Median Follow-Up (months)	Median OS in Intervention Arm (months)	Median OS in Control Arm (months)	Group: HR (95% CI)
ARASENS ^{13,14}	1,306	ADT plus docetaxel plus darolutamide	ADT plus docetaxel plus placebo	86	77	43.7	NR	48.9	Overall: 0.68 (0.57 to 0.80) Synchronous + HV: 0.69 (0.57 to 0.85) Synchronous + LV: 0.75 (0.45 to 1.27) Metachronous + HV: 0.69 (0.39 to 1.24) Metachronous + LV: NA
PEACE-1 (docetaxel subgroup) ¹⁵	710	SOC plus abiraterone (with or without RT)	SOC (with or without RT)	100	64	45.6	NR	53.2	Overall (all synchronous): 0.75 (0.59 to 0.95)
ENZAMET (docetaxel subgroup) ¹⁶	503	ADT plus docetaxel plus enzalutamide	ADT plus docetaxel plus NSAA	72	71	68 (overall cohort)	Not reported	Not reported	Synchronous (all): 0.73 (0.55 to 0.99) Synchronous + HV: 0.79 (0.57 to 1.10) Synchronous + LV: 0.57 (0.29 to 1.12) Metachronous (all): 1.10 (0.65 to 1.86)

Abbreviations: ADT, androgen deprivation therapy; HR, hazard ratio; HV, high-volume; LV, low-volume; NA, not applicable; NR, not reached; OS, overall survival; RT, radiotherapy; SOC, standard of care.

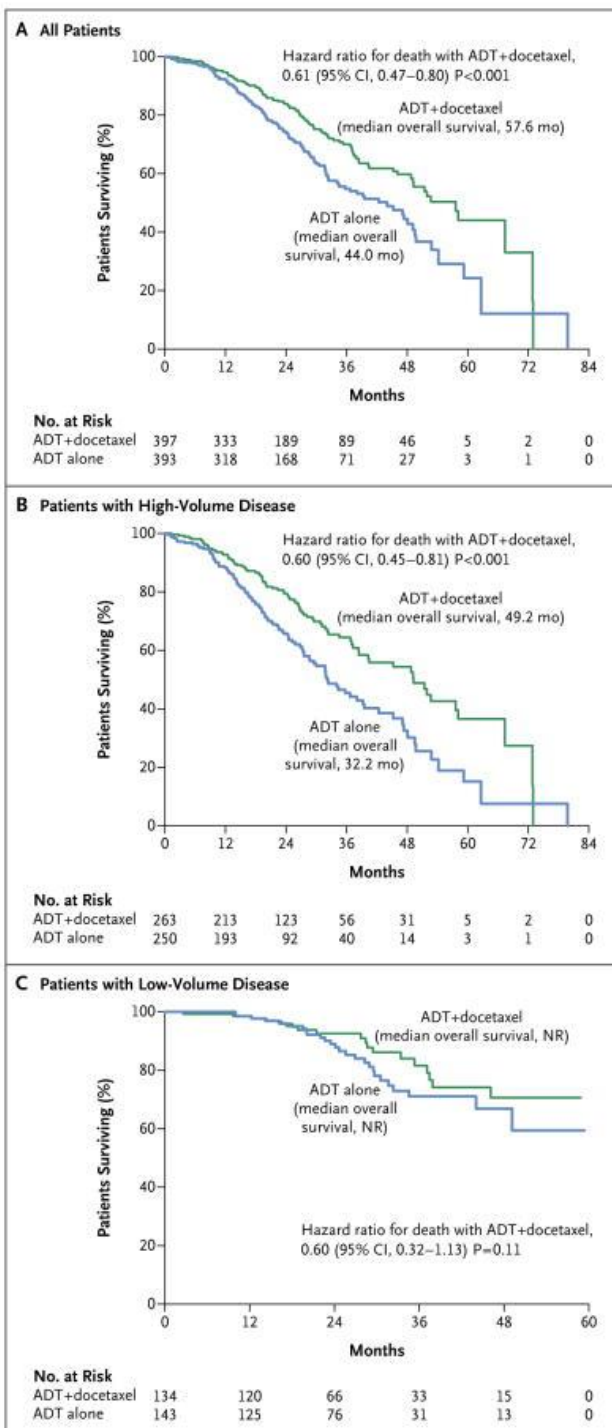
Prostatakarzinom

hormonsensitiv - Docetaxel



Prostatakarzinom

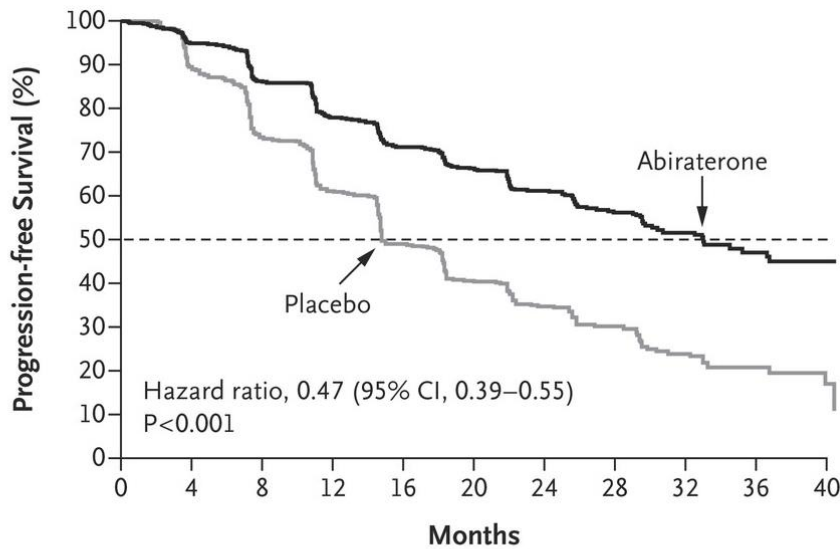
hormonsensitiv - Docetaxel



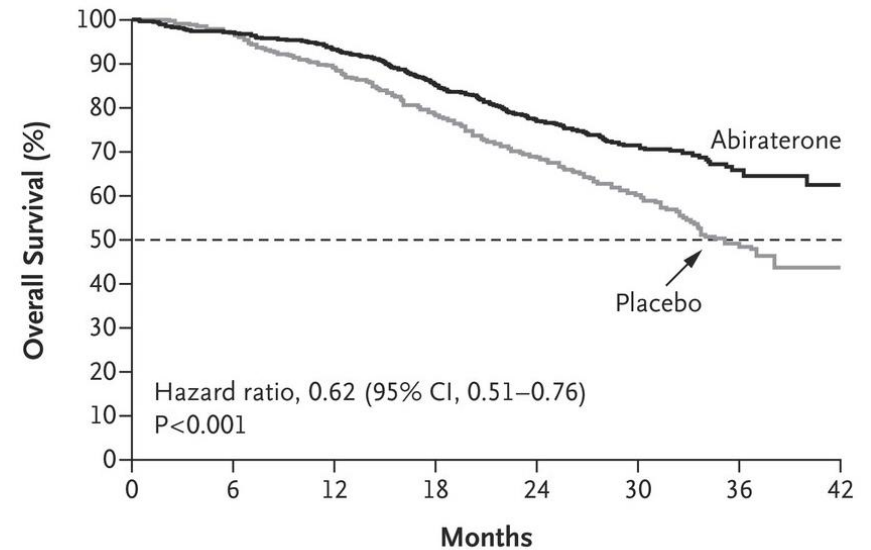
Prostatakarzinom

hormonsensitiv, hohes Risiko - Abirateron

Hochrisiko
Gleason >8
≥3 Knochenmetastasen
„viszerale“ Metastasen (Lunge, Leber, ...)



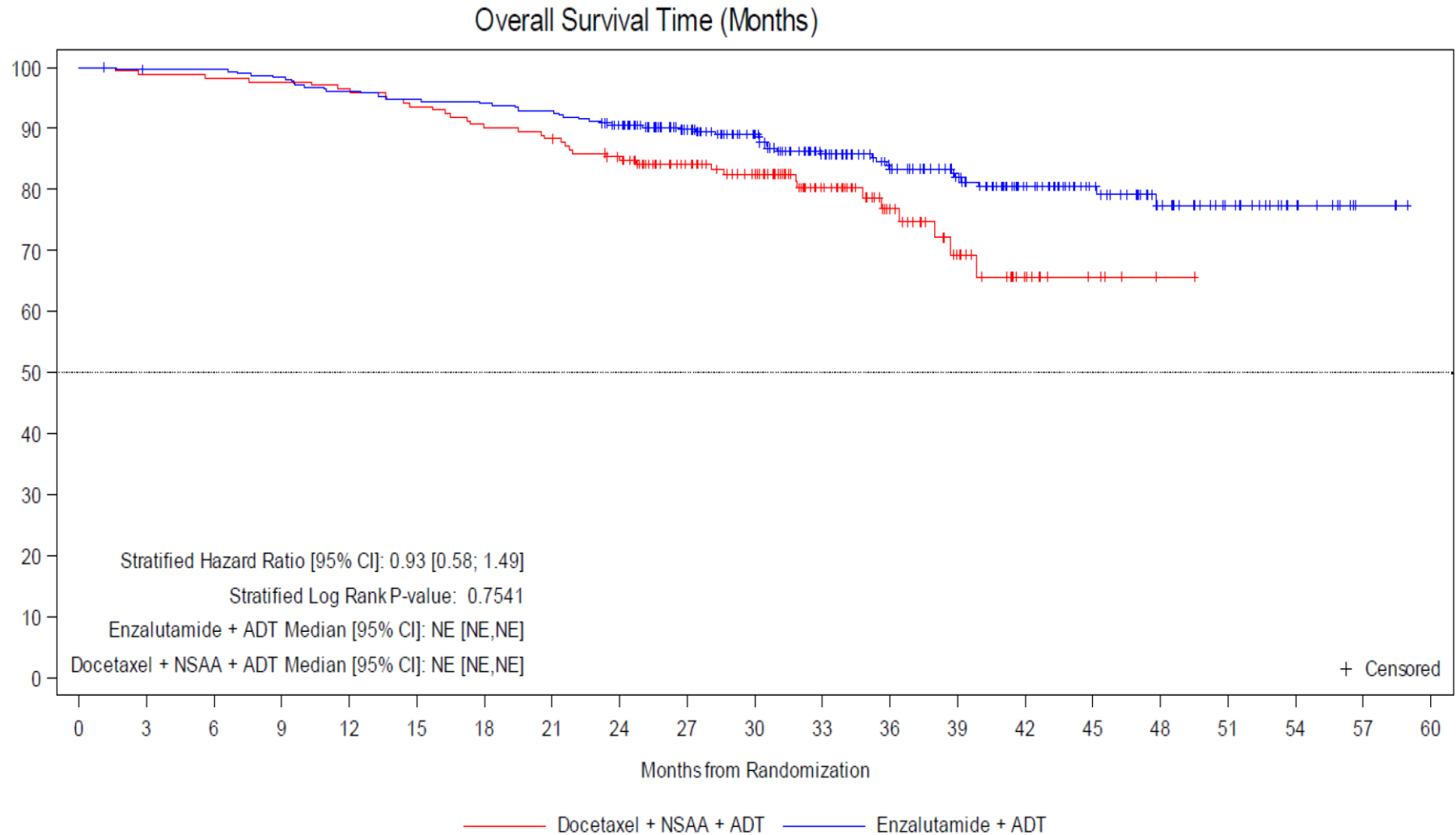
No. at Risk	0	4	8	12	16	20	24	28	32	36	40
Abiraterone	597	533	464	400	353	316	251	177	102	51	21
Placebo	602	488	367	289	214	168	127	81	41	17	7



No. at Risk	0	6	12	18	24	30	36	42
Abiraterone	597	565	529	479	388	233	93	9
Placebo	602	564	504	432	332	172	57	2

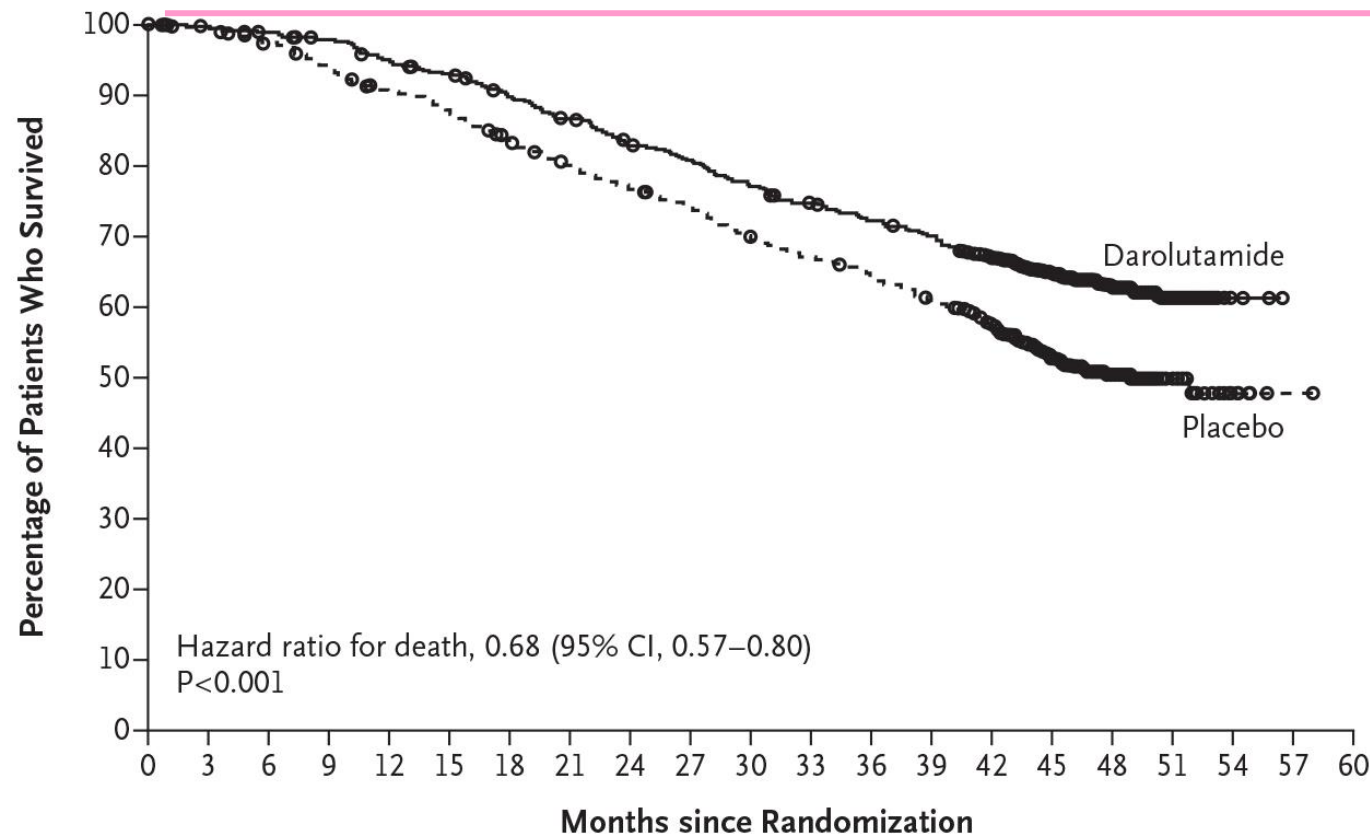
Prostatakarzinom

hormonsensitiv - Enzalutamid



Prostatakarzinom

hormonsensitiv, hohes Risiko – Darolutamid + Docetaxel

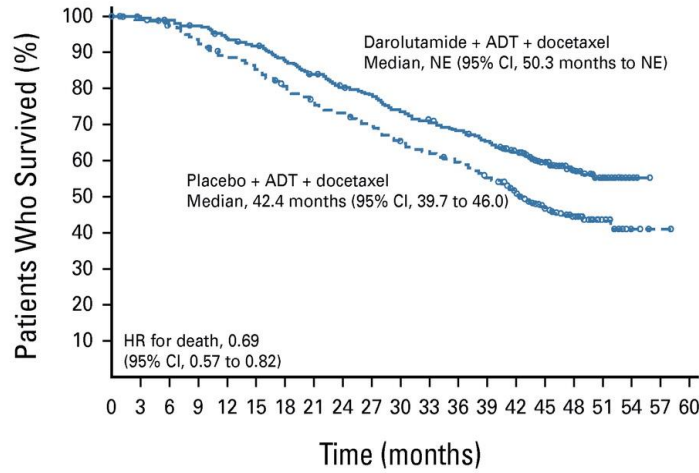


No. at Risk

Darolutamid	651	645	637	627	608	593	570	548	525	509	486	468	452	436	402	267	139	56	9	0	0
Placebo	654	646	630	607	580	565	535	510	488	470	441	424	402	383	340	218	107	37	6	1	0

High Volume

A

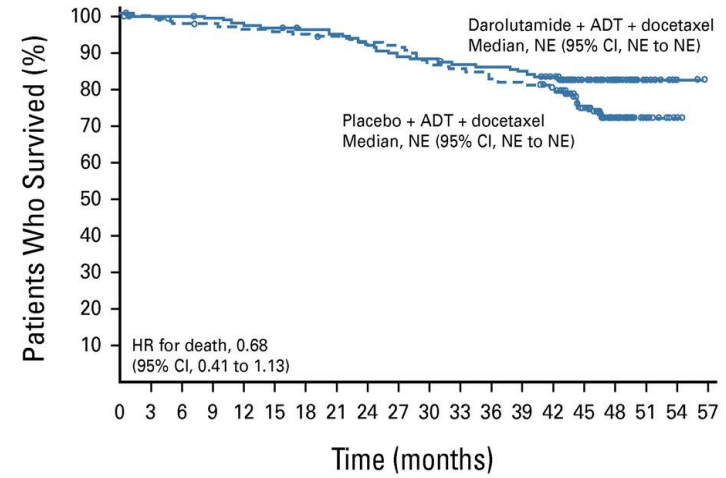


No. of high-volume patients at risk:

Darolutamide	497	494	486	479	462	449	429	408	389	378	356	341	326	312	285	193	103	43	6	0	0
Placebo	508	502	491	469	444	430	401	378	358	341	319	304	286	269	233	153	72	23	4	1	0

Low Volume

B

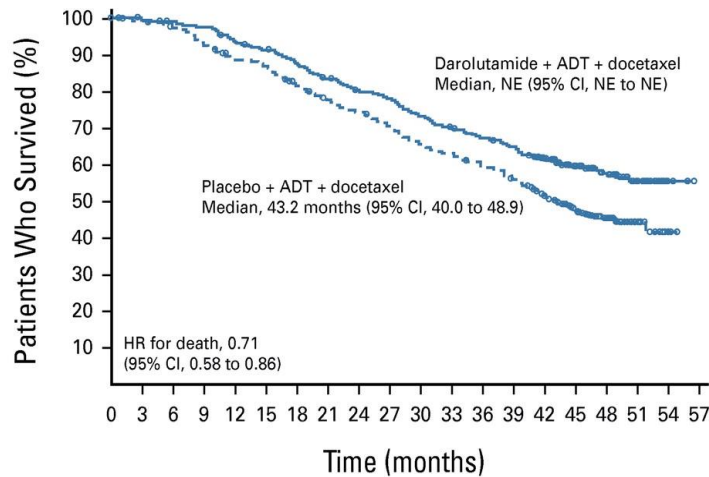


No. of low-volume patients at risk:

Darolutamide	154	151	151	148	146	144	141	140	136	131	130	127	126	124	117	74	36	13	3	0
Placebo	146	144	139	138	136	135	134	132	130	129	122	120	116	114	107	65	35	14	2	0

High Risk

C

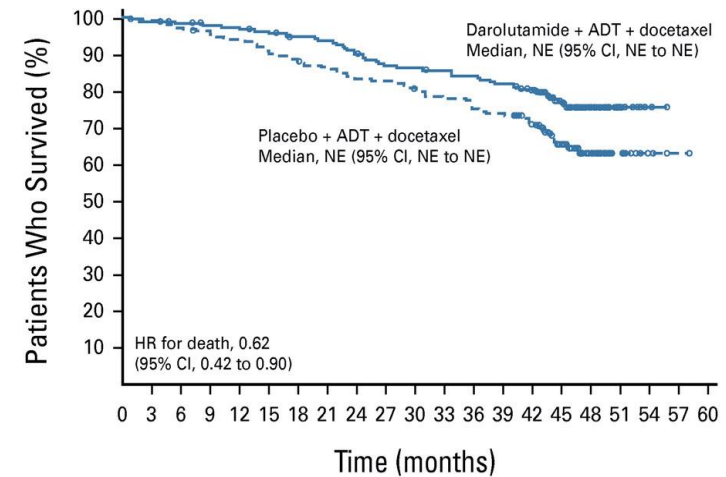


No. of high-risk patients at risk:

Darolutamide	452	450	443	437	419	407	389	369	352	344	322	308	294	282	257	177	99	42	6	0
Placebo	460	453	443	423	400	392	367	346	330	313	290	277	261	245	215	148	72	24	3	0

Low Risk

D



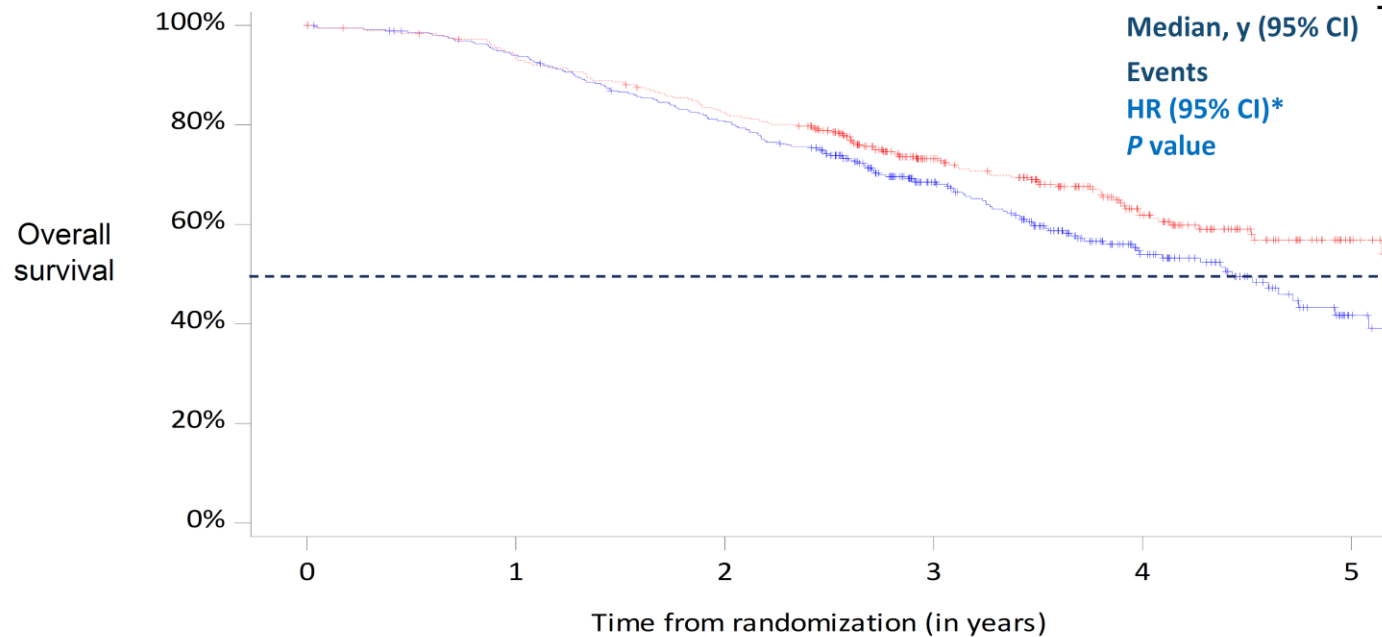
No. of low-risk patients at risk:

Darolutamide	199	195	194	190	189	186	181	179	173	165	164	160	158	154	145	90	40	14	3	0	0
Placebo	194	193	187	184	180	173	168	164	158	157	151	147	141	138	125	70	35	13	3	1	0

Prostatakarzinom

hormonsensitiv – TRIPLE Therapie

OS with Abiraterone in the ADT+docetaxel (+/-RXT) population



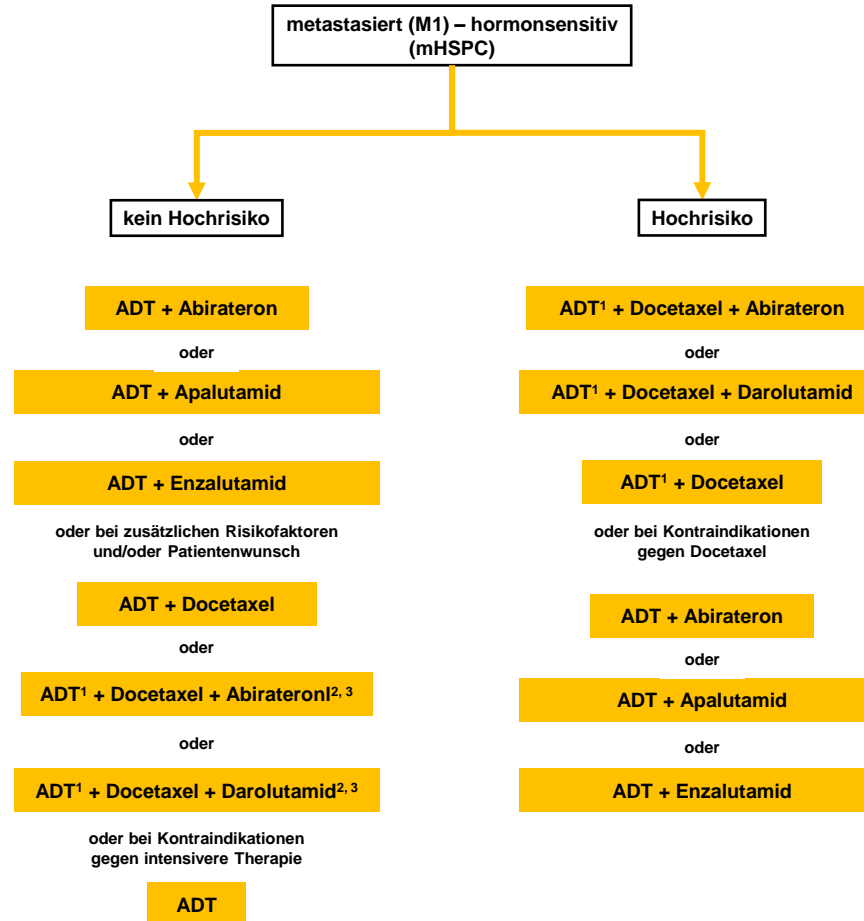
	SOC+Abi (n = 355)	SOC (n = 355)
Median, y (95% CI)	NE (4.5-NE)	4.4 (3.8-4.9)
Events	121	151
HR (95% CI)*	0.75 (0.59-0.95)	
P value	0.017	

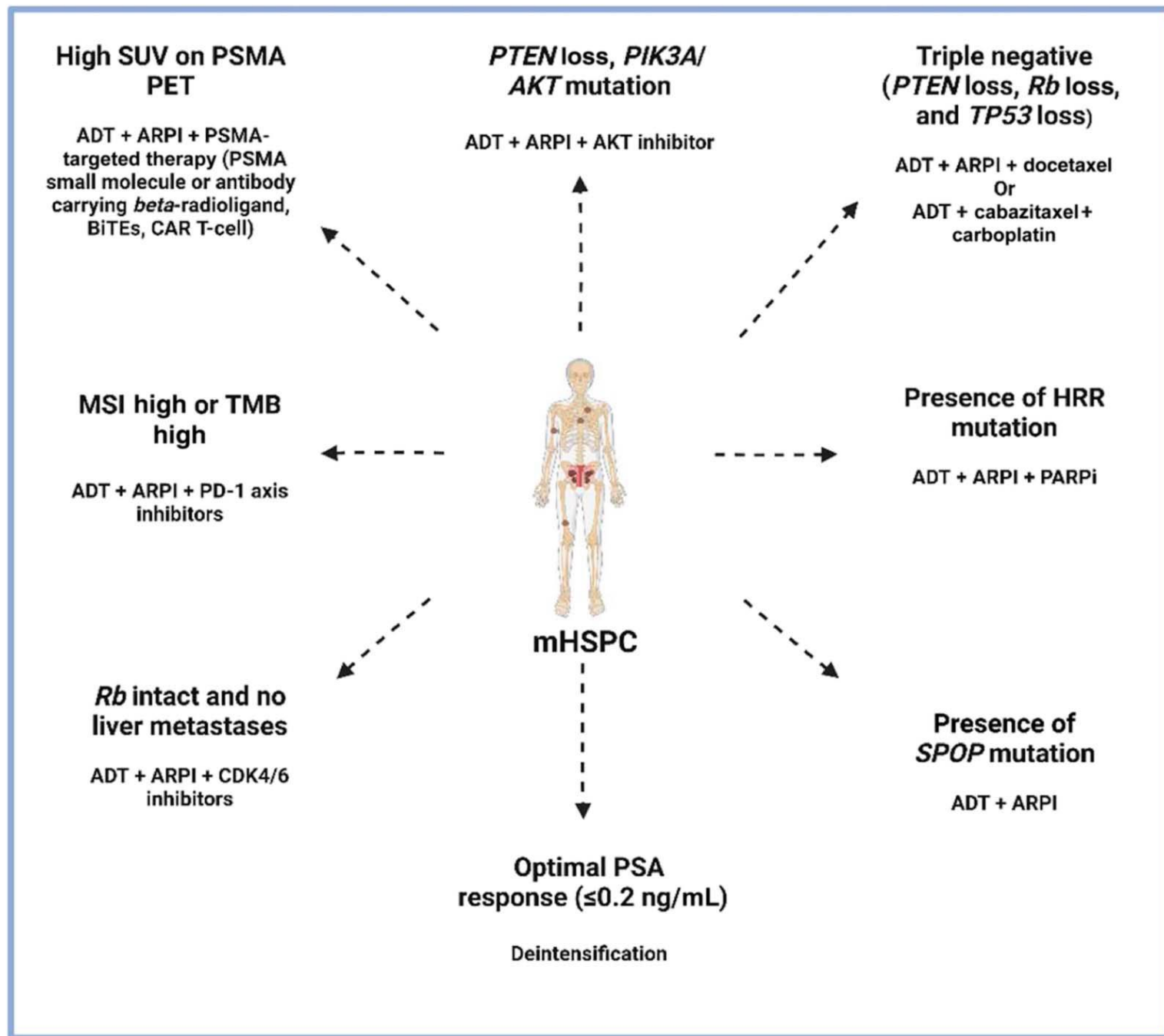
	No	Yes
No	355	329
Yes	355	328

*Adjusted on stratification parameters (RXT, type of castration, PS, metastatic burden)

Prostatakarzinom

hormonsensitiv metastasiert





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Vielen Dank für Ihre Aufmerksamkeit!

