Orazio Caffo

XVIII CONGRESSO
DI ONCOLOGIA TREVIGLIESE
Un incidente
di percorso

Unità Operativa
di Oncologia Medica
Ospedale di Trento

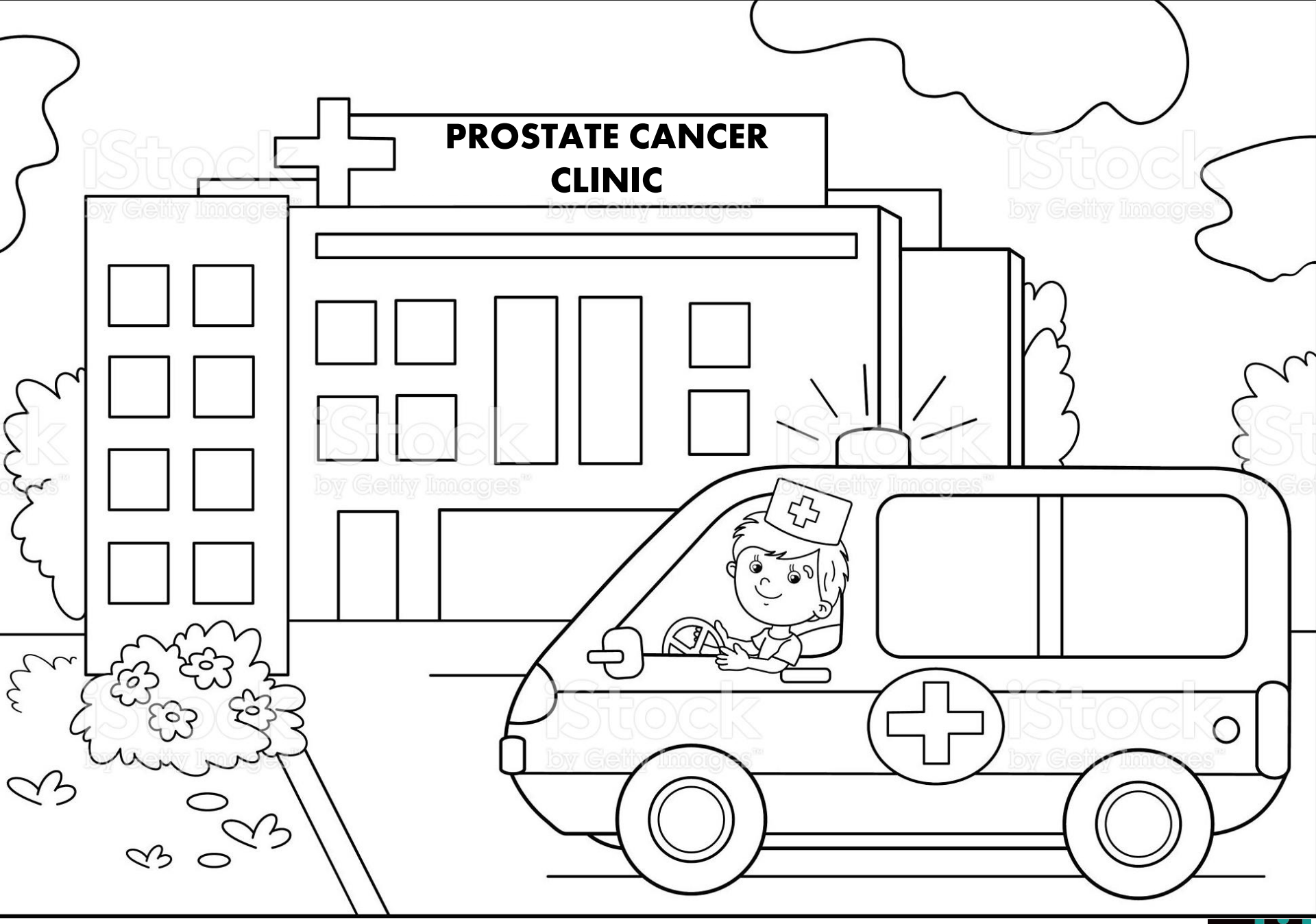
Disclosures

- Consultant
  - Astellas
  - Janssen
  - Sanofi
- Speaker
  - Astellas
  - Bayer
  - Janssen
  - Sanofi

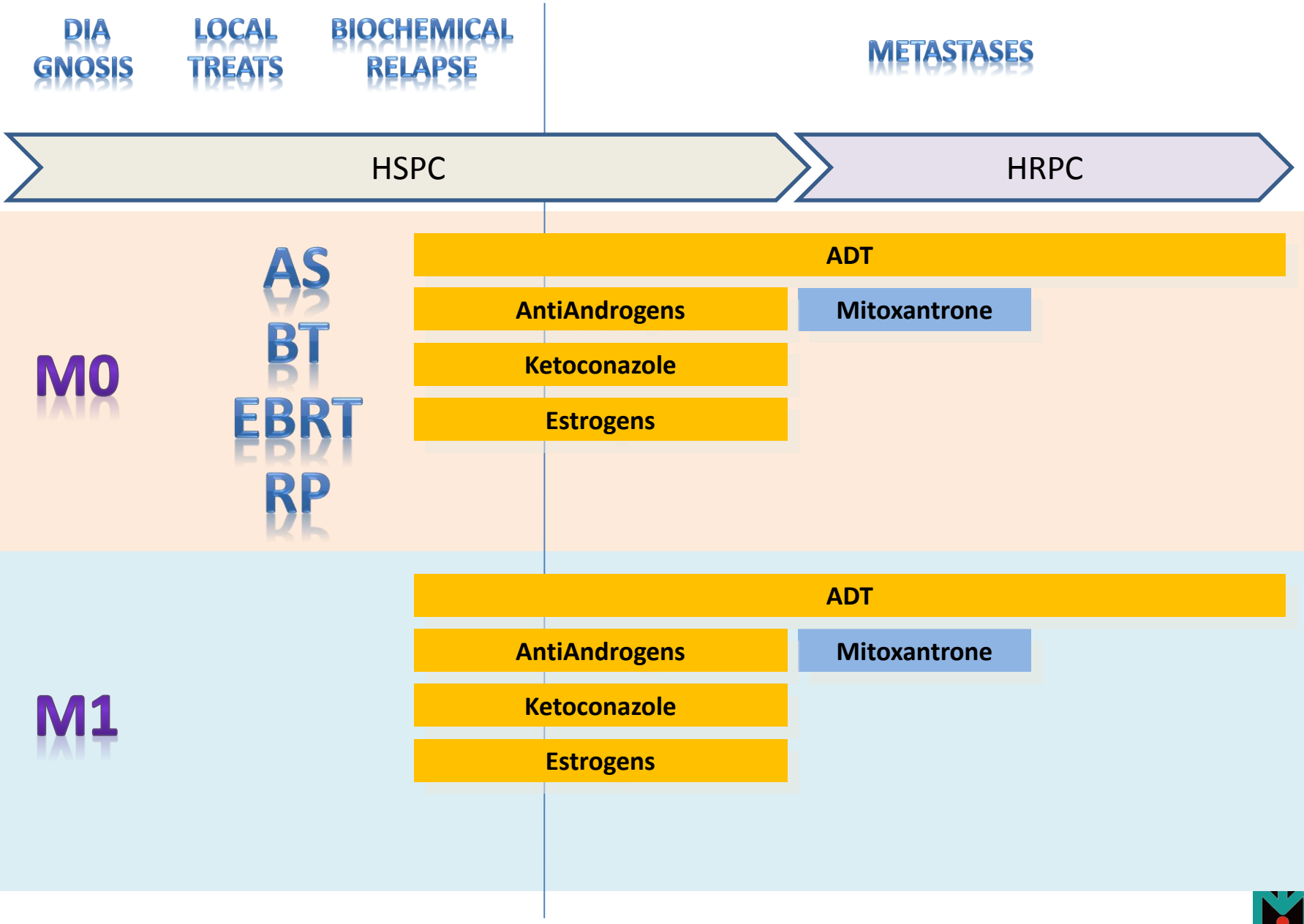
XVIII CONGRESSO
DI ONCOLOGIA TREVIGLIESE

Un incidente
di percorso

Unità Operativa
di Oncologia Medica
Ospedale di Trento


PROSTATE CANCER
CLINIC

15 years ago


DIA GNOSIS
LOCAL TREATS
BIOCHEMICAL RELAPSE
METASTASES
HSPC
HRPC
M0
AS
BT
EBRT
RP
ADT
AntiAndrogens
Mitoxantrone
Ketoconazole
Estrogens
M1
ADT
AntiAndrogens
Mitoxantrone
Ketoconazole
Estrogens

today

DIA GNOSIS

LOCAL TREATS

BIOCHEMICAL RELAPSE

METASTASES

CSPC

CRPC

M0

AS

BT

EBRT

RP

ADT

AntiAndrogens

Abiraterone

Abiraterone

Enzalutamide

Enzalutamide

Docetaxel

Cabazitaxel

Radium 223

M1

ADT

Abiraterone

Abiraterone

Enzalutamide

Enzalutamide

Docetaxel

Cabazitaxel

Radium 223

mCRPC front line

drug	comparator	OS Δ	HR	p
docetaxel	MITOX	2.5 mos	0.76	<0.001
abiraterone	PLACEBO+PDN	4.4 mos	0.81	0.003
enzalutamide	PLACEBO	2.2 mos	0.71	<0.001
radium-223	PLACEBO	4.6 mos	0.74	0.03

mCRPC second line

drug	comparator	OS Δ	HR	p
cabazitaxel	MITOX	2.4 mos	0.70	<0.001
abiraterone	PLACEBO+PDN	3.9 mos	0.65	<0.001
enzalutamide	PLACEBO	4.8 mos	0.63	<0.001
radium 223	PLACEBO	3.1 mos	0.71	0.003

Impact of news drugs in the median overall survival of patients with metastatic castration resistant prostate cancer (mCRPC)

N. Chaumard-Billotey [1], M. Aitichou [1], S. Chabaud [2], H. Boyle [3], B. Favier [1], Y. Devaux [3], JP. Droz [3], A. Fléchon [3]

[1] Pharmacy department, [2] Biostatistical unit, [3] Department of Oncology - Centre Léon Bérard, 28 Rue Laennec, Lyon 69008, France.

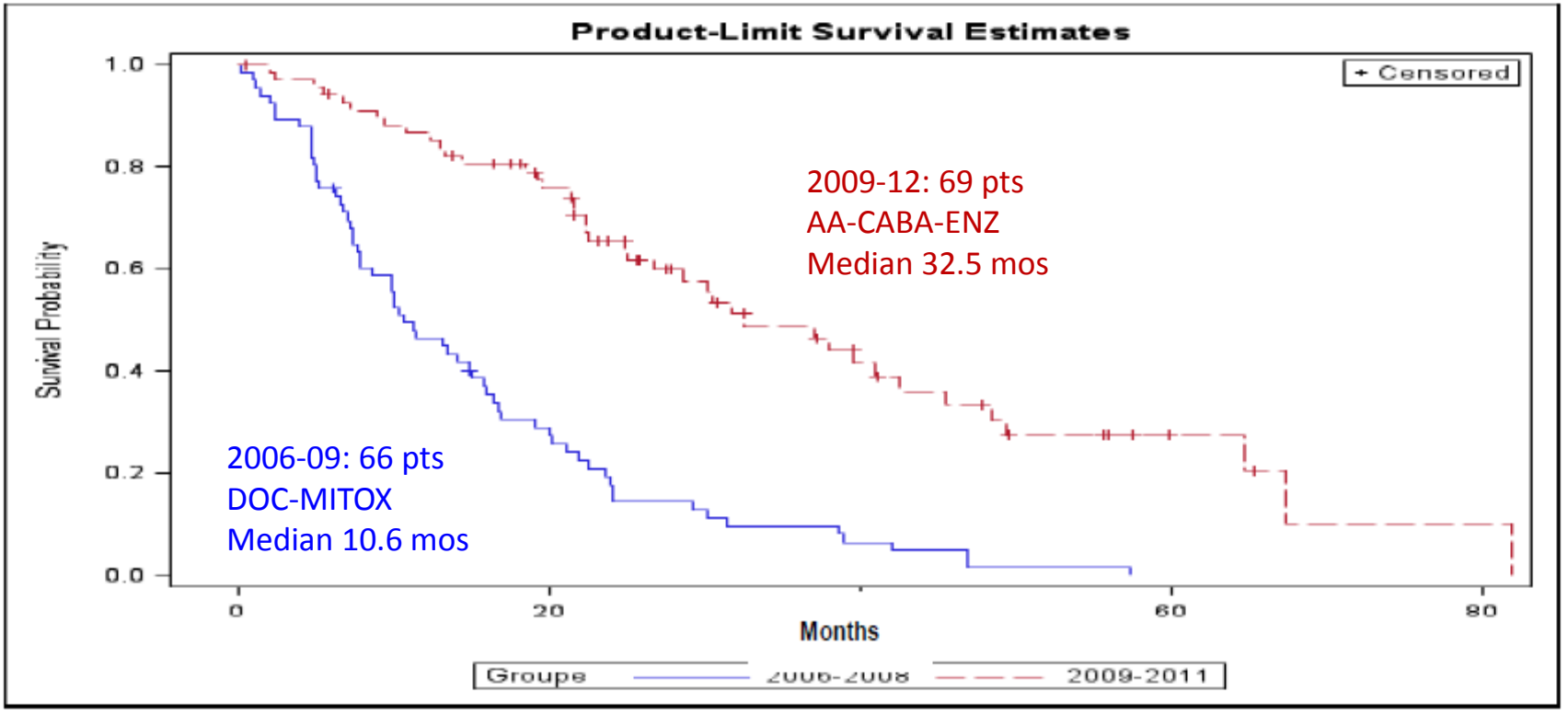
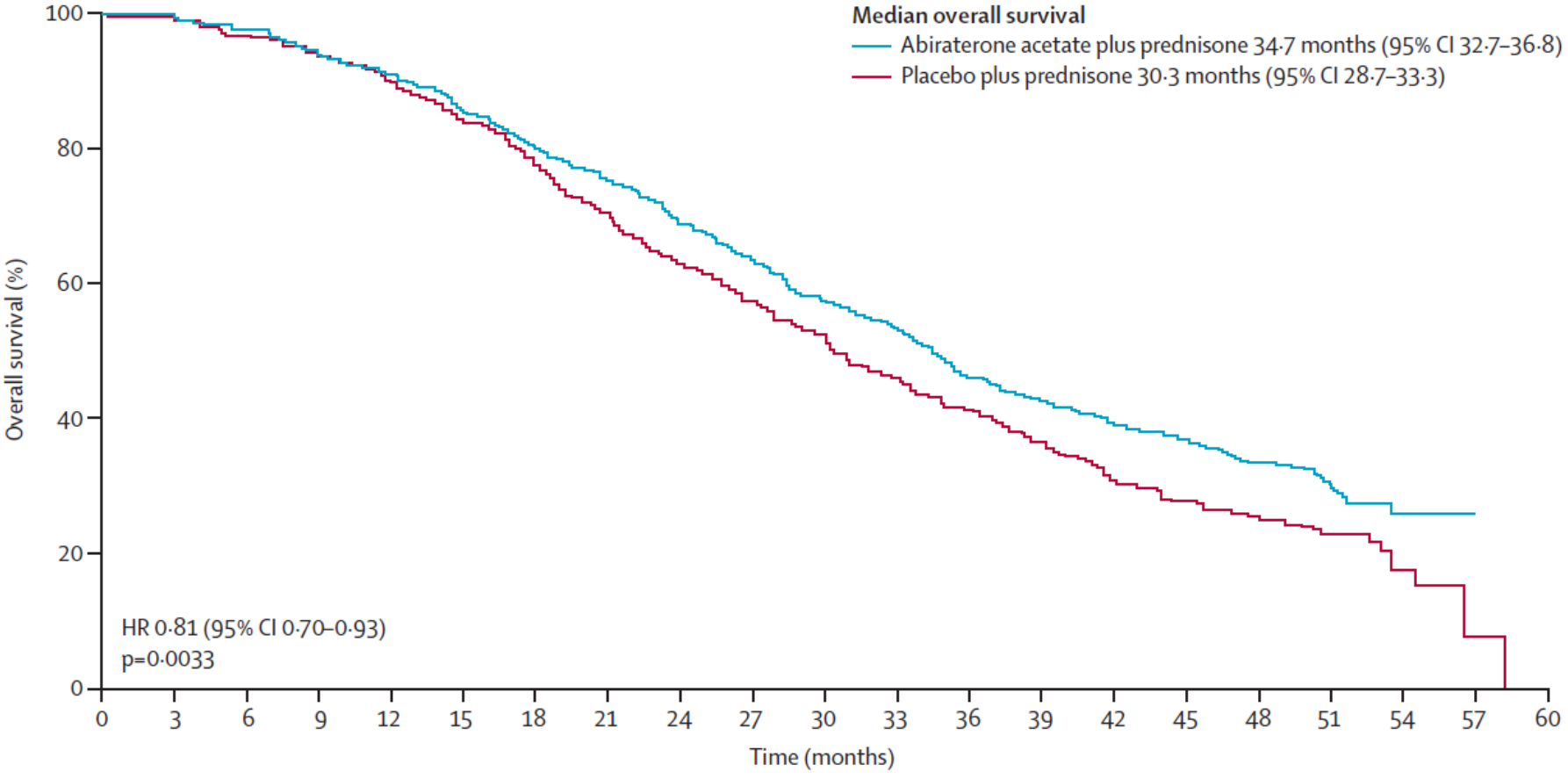


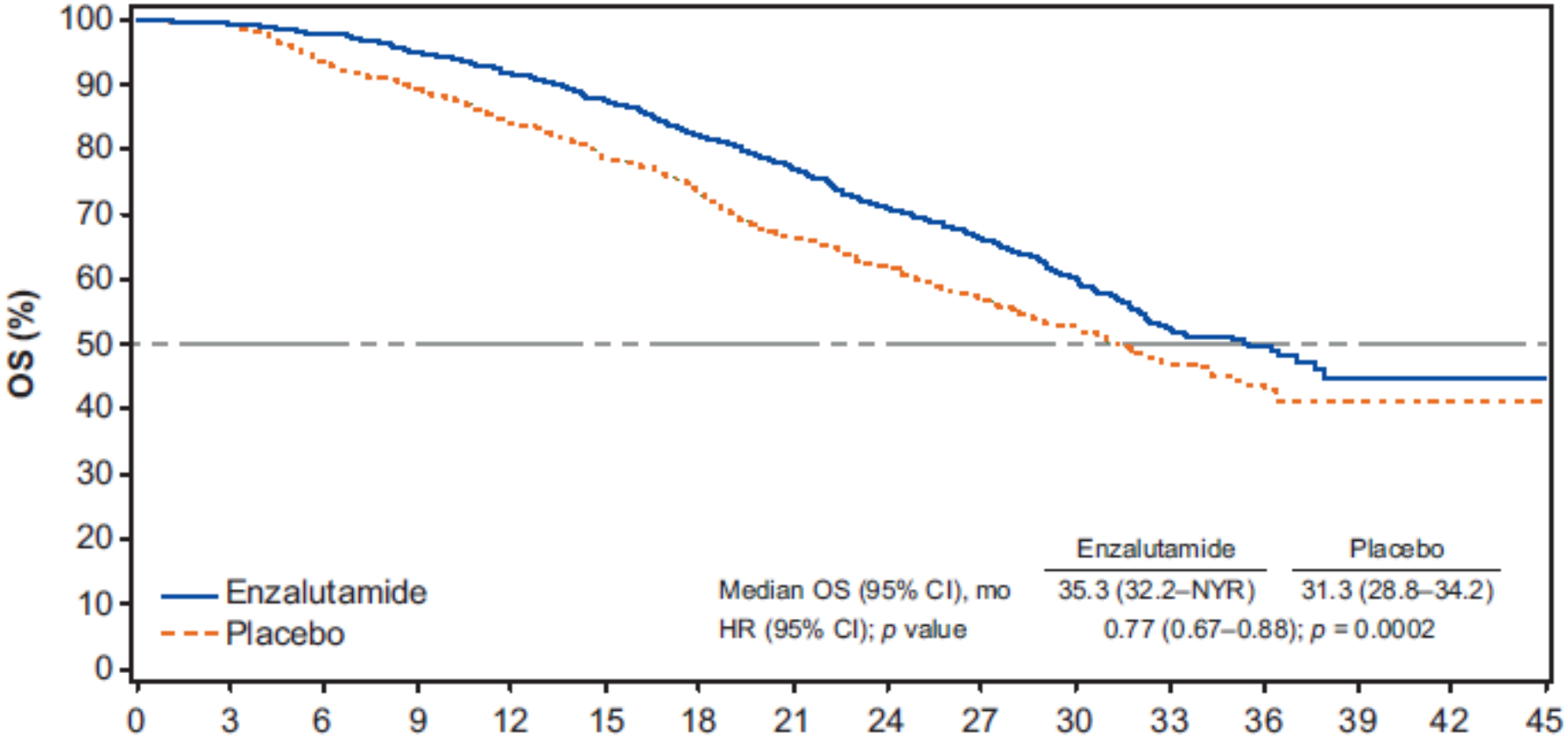
Figure 1 : Overall survival of mCRPC patients according to the period of treatment

Patient characteristics remained comparable during the two periods.
Nevertheless, over time, survival has improved obviously, probably through earlier management, more intensive schedules of docetaxel and use of new drugs.

COU-AA 302 OS analysis (final)



PREVAIL OS analysis



THE PROBLEM OF SEQUENCING THE NEW AGENTS

Different strategic drivers

- To use first all “low impact” treatments
  - To maximize chemo dilation
- To use first all “aggressive” treatments
  - To exploit better performance status in early phases
- To mix agents with different mechanisms of action
  - To avoid cross resistance

What we know

- The disease control is progressively reduced by treatment line
- The pts' PS progressively worsens by treatment line

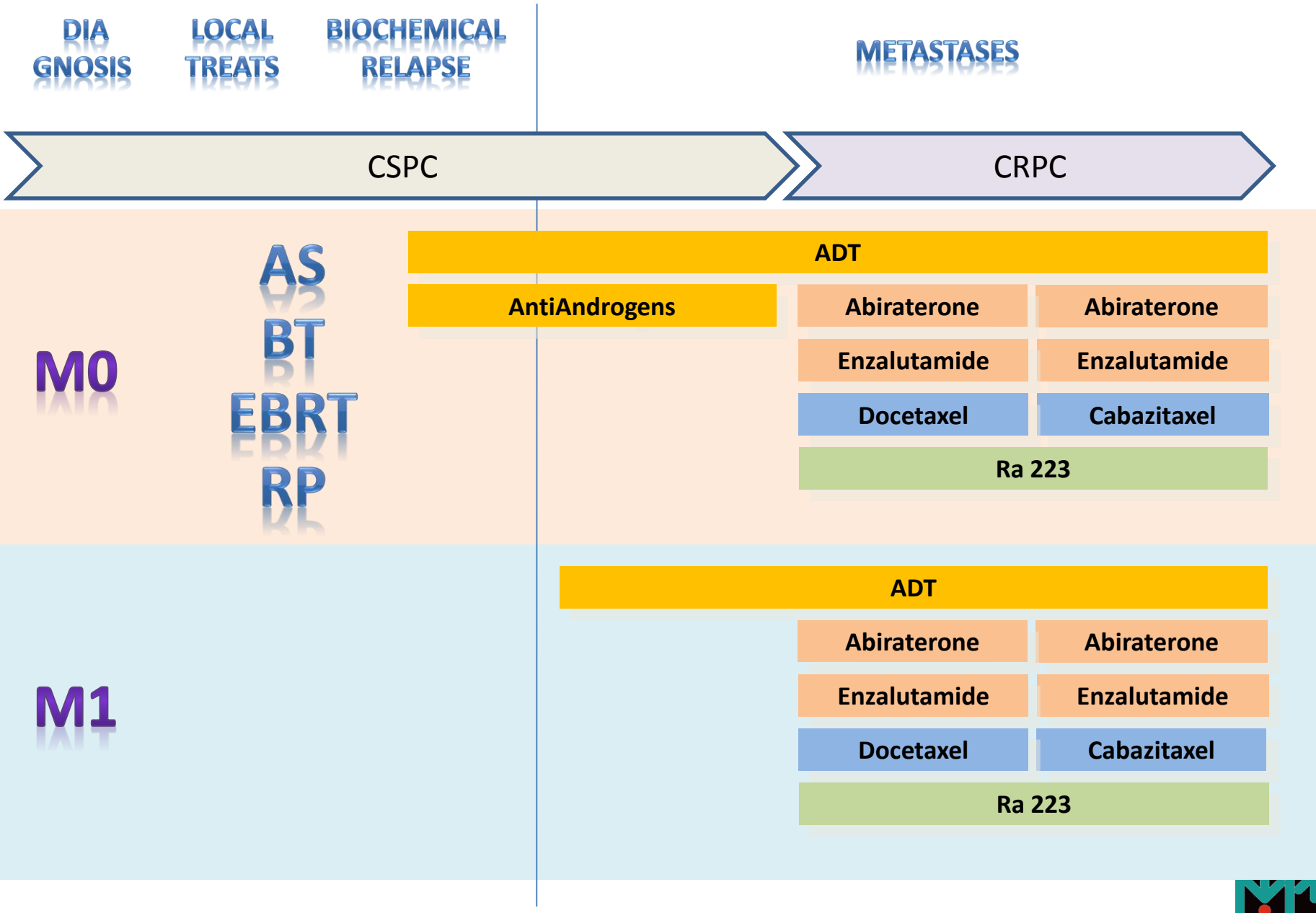
What we do not know

- Cross resistance
- Changes in disease biology as response to the treatments
- Agents activity after the exposure of other agents (different from those used in pivotal trials)

BUT……

THE LANDSCAPE IS RAPIDLY EVOLVING

today


DIA GNOSIS
LOCAL TREATS
BIOCHEMICAL RELAPSE
METASTASES
CSPC
CRPC
M0
AS
BT
EBRT
RP
ADT
AntiAndrogens
Abiraterone
Abiraterone
Enzalutamide
Enzalutamide
Docetaxel
Cabazitaxel
Ra 223
M1
ADT
Abiraterone
Abiraterone
Enzalutamide
Enzalutamide
Docetaxel
Cabazitaxel
Ra 223

today

DIA GNOSIS | LOCAL TREATS | BIOCHEMICAL RELAPSE | METASTASES

CSPC | CRPC

M0

AS
BT
EBRT
RP

- ADT
  - AntiAndrogens
  - Abiraterone
  - Enzalutamide
  - Docetaxel
  - Abiraterone
  - Enzalutamide
  - Cabazitaxel
  - Ra 223

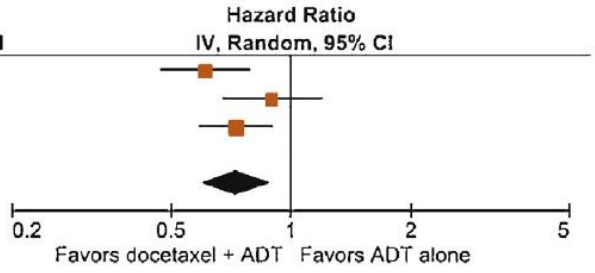
M1

- ADT
  - Abiraterone
  - Docetaxel
  - Abiraterone
  - Enzalutamide
  - Docetaxel
  - Abiraterone
  - Enzalutamide
  - Cabazitaxel
  - Ra 223

A

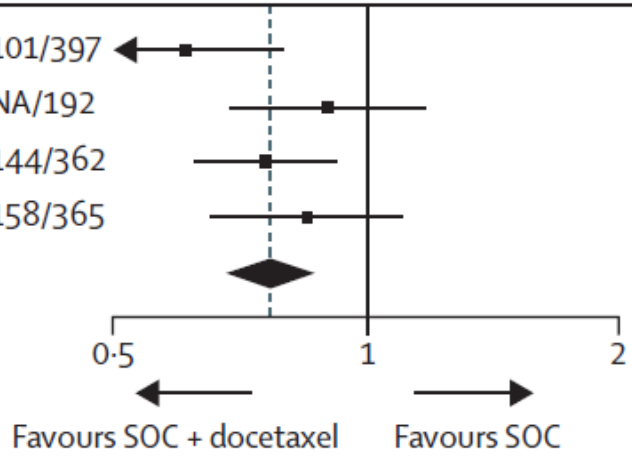
Study or Subgroup	log[Hazard Ratio]	SE	Docetaxel + ADT Total	ADT alone Total	Weight	Hazard Ratio IV, Random, 95% CI
CHAARTED	-0.4943	0.133	397	393	32.1%	0.61 [0.47, 0.79]
GETUG-AFU 15	-0.1054	0.1468	192	193	28.8%	0.90 [0.67, 1.20]
STAMPEDE Docetaxel	-0.3147	0.1086	362	725	39.1%	0.73 [0.59, 0.90]
Total (95% CI)			**951**	**1311**	**100.0%**	**0.73 [0.60, 0.90]**

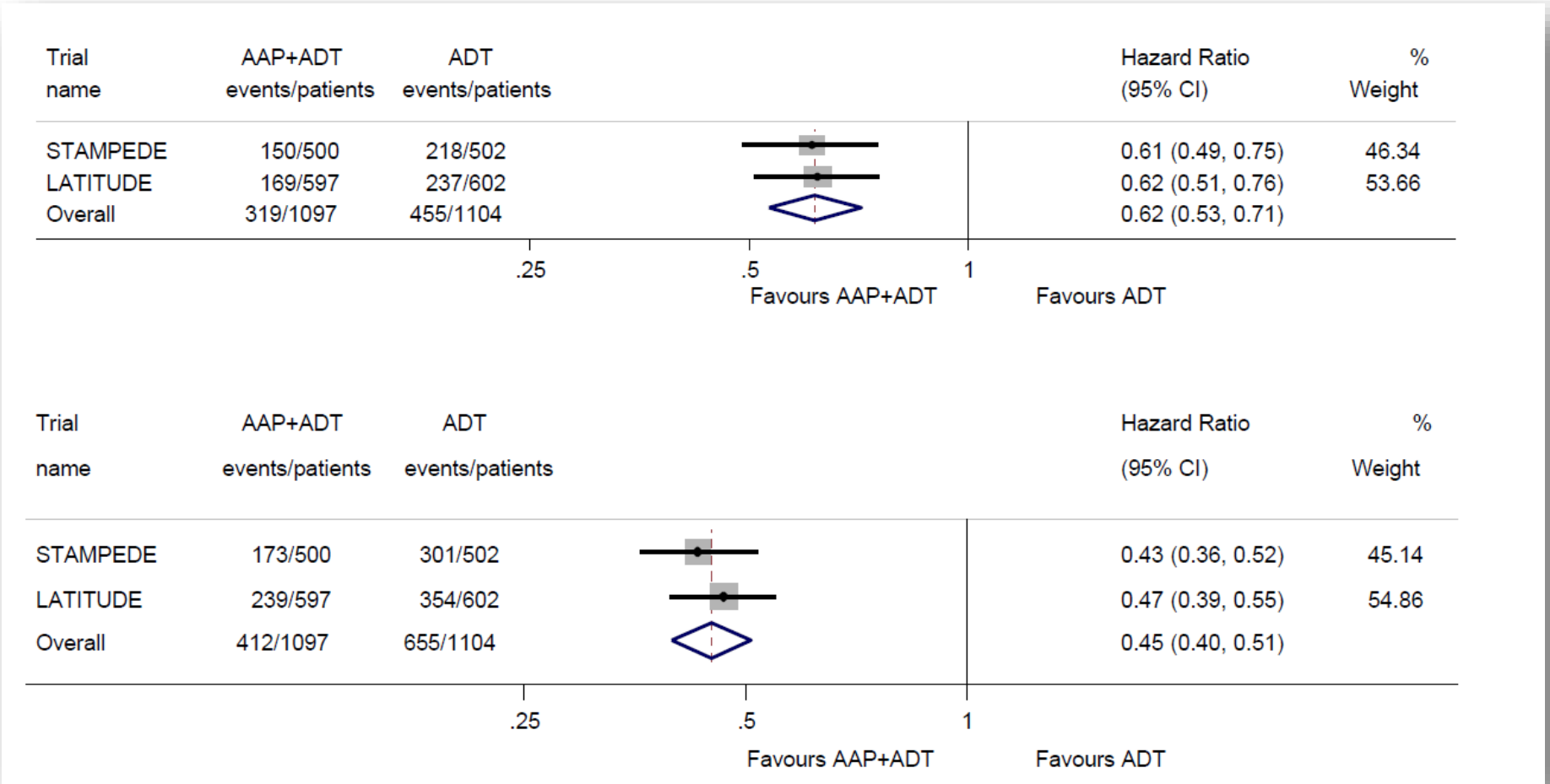
Heterogeneity: Tau² = 0.02; Chi² = 3.86, df = 2 (P = 0.15); I² = 48%
Test for overall effect: Z = 3.03 (P = 0.002)



	Control	Treatment	Hazard ratio (95% CI)
CHAARTED[7]	136/393	101/397	0·61 (0·47–0·80)
GETUG-15[9,10]	NA/193	NA/192	0·90 (0·69–1·81)
STAMPEDE[8] (SOC +/– Doc)	350/724	144/362	0·76 (0·62–0·93)
STAMPEDE[8] (SOC + ZA +/– Doc)	170/366	158/365	0·85 (0·65–1·10)
Overall			**0·77 (0·68–0·87)**

Heterogeneity: χ^2=4·80; df=3; p=0·187; I^2=37·5%



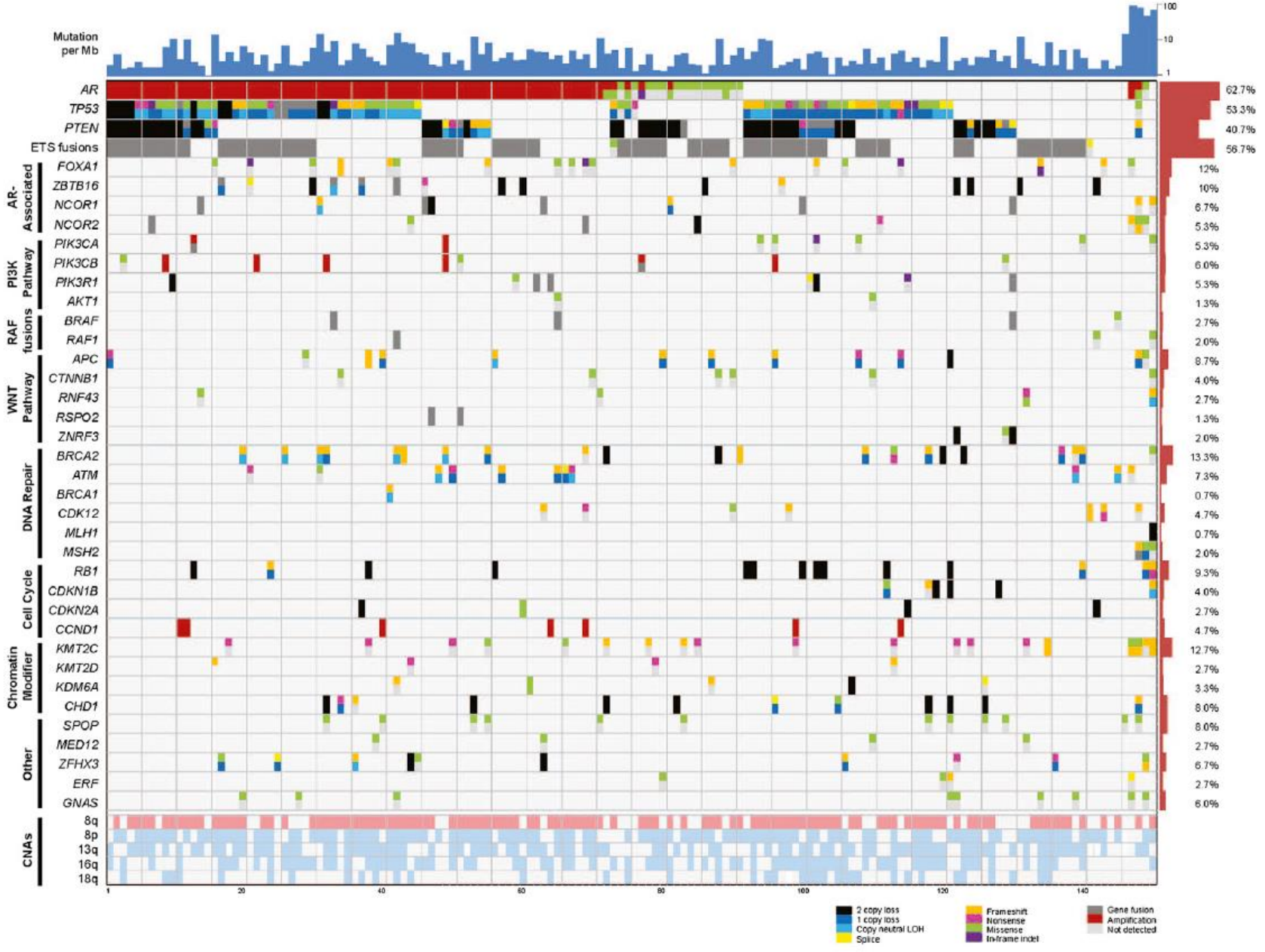

Trial name
AAP+ADT events/patients
ADT events/patients
Hazard Ratio (95% CI)
% Weight
STAMPEDE 150/500 218/502 0.61 (0.49, 0.75) 46.34
LATITUDE 169/597 237/602 0.62 (0.51, 0.76) 53.66
Overall 319/1097 455/1104 0.62 (0.53, 0.71)
.25
.5
1
Favours AAP+ADT
Favours ADT
Trial name
AAP+ADT events/patients
ADT events/patients
Hazard Ratio (95% CI)
% Weight
STAMPEDE 173/500 301/502 0.43 (0.36, 0.52) 45.14
LATITUDE 239/597 354/602 0.47 (0.39, 0.55) 54.86
Overall 412/1097 655/1104 0.45 (0.40, 0.51)
.25
.5
1
Favours AAP+ADT
Favours ADT

today the question is:

DOC or AA in CSPC?

the future around the corner:

precision medicine



Robinson et al Cell 2015

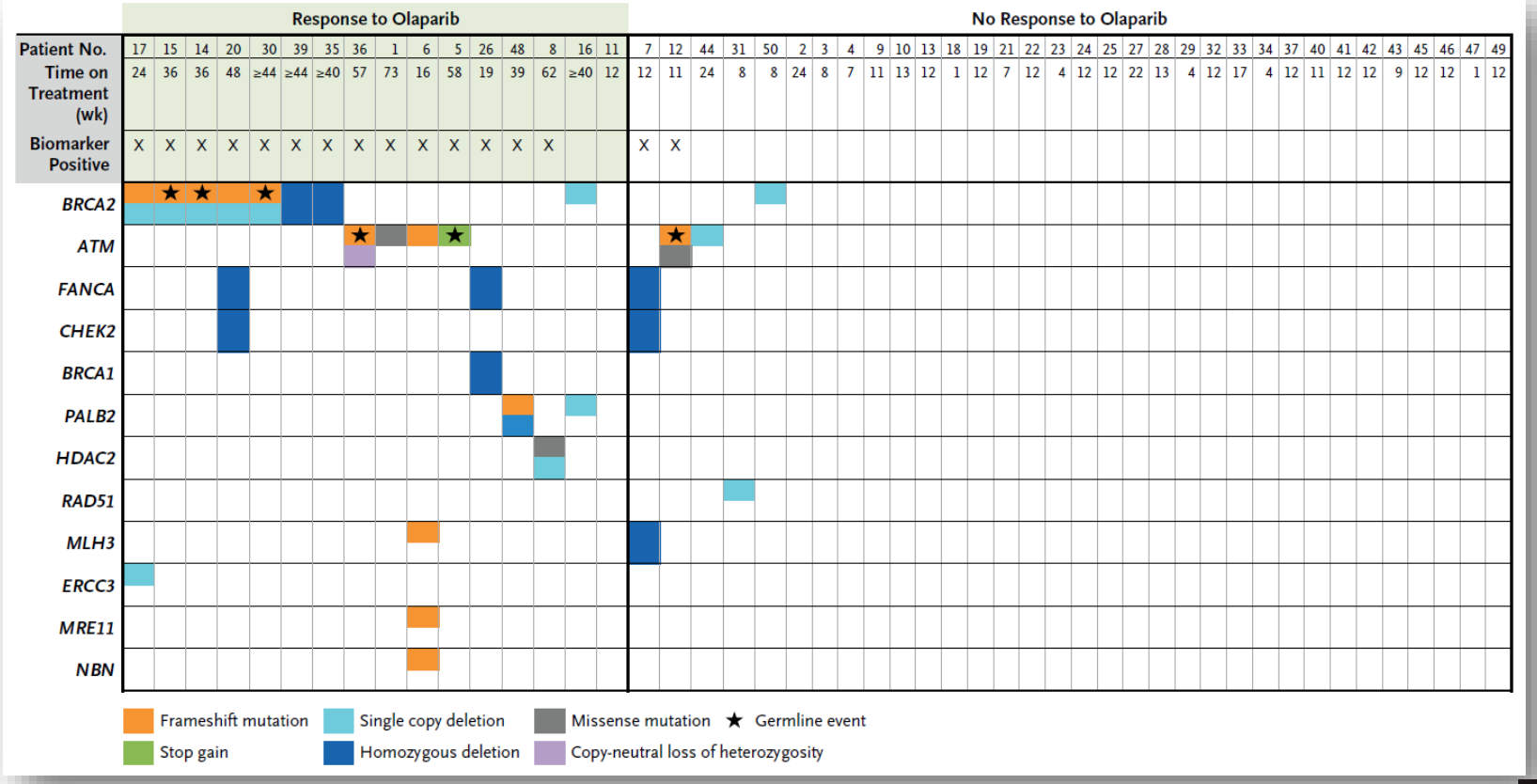
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 29, 2015 VOL. 373 NO. 18

DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer

J. Mateo, S. Carreira, S. Sandhu, S. Miranda, H. Mossop, R. Perez-Lopez, D. Nava Rodrigues, D. Robinson, A. Omlin, N. Tunariu, G. Boysen, N. Porta, P. Flohr, A. Gillman, I. Figueiredo, C. Paulding, G. Seed, S. Jain, C. Ralph, A. Protheroe, S. Hussain, R. Jones, T. Elliott, U. McGovern, D. Bianchini, J. Goodall, Z. Zafeiriou, C.T. Williamson, R. Ferraldeschi, R. Riisnaes, B. Ebbs, G. Fowler, D. Roda, W. Yuan, Y.-M. Wu, X. Cao, R. Brough, H. Pemberton, R. A'Hern, A. Swain, L.P. Kunju, R. Eeles, G. Attard, C.J. Lord, A. Ashworth, M.A. Rubin, K.E. Knudsen, F.Y. Feng, A.M. Chinnaiyan, E. Hall, and J.S. de Bono

TOPARP-A



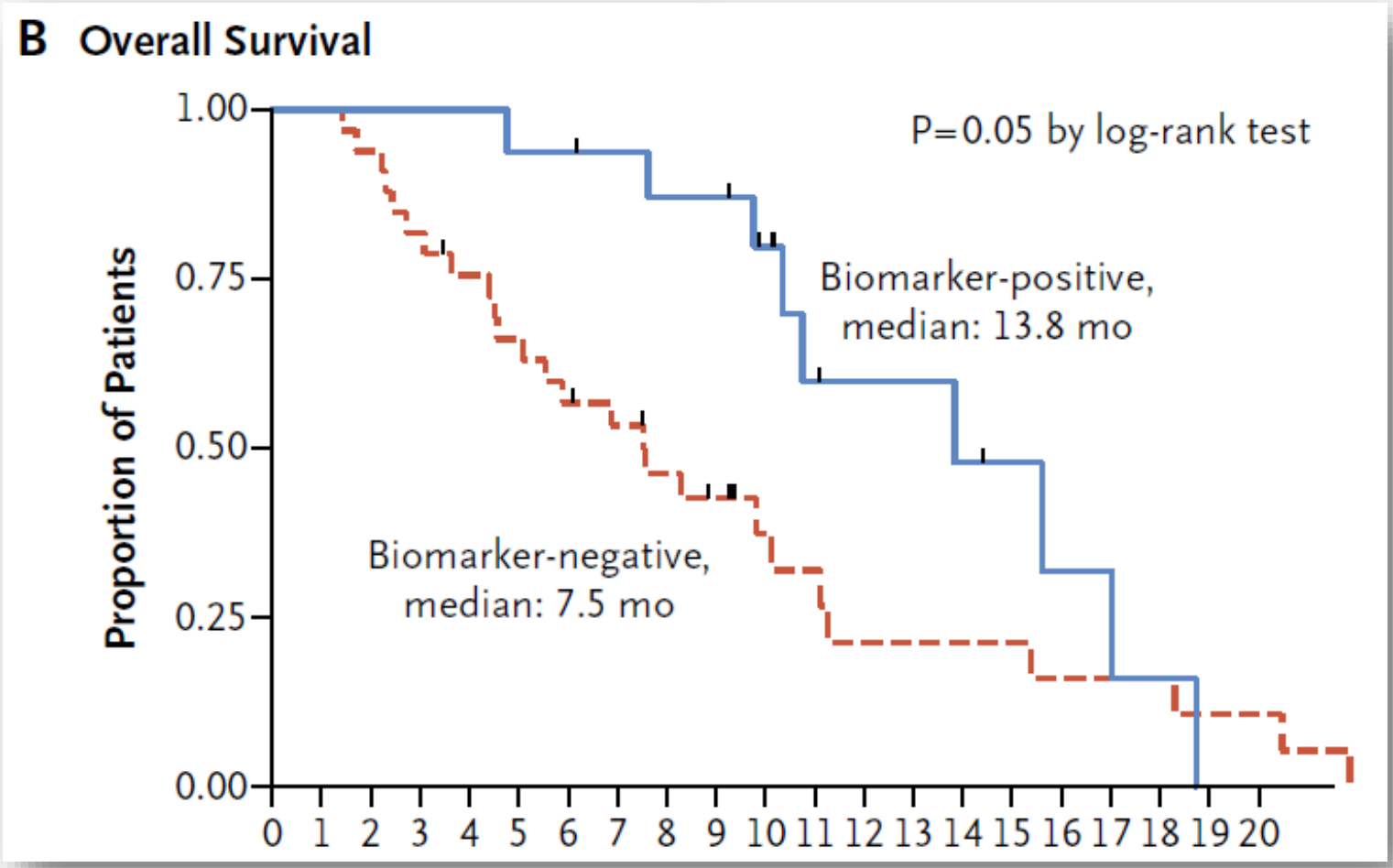
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 29, 2015 VOL. 373 NO. 18

DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer

J. Mateo, S. Carreira, S. Sandhu, S. Miranda, H. Mossop, R. Perez-Lopez, D. Nava Rodrigues, D. Robinson, A. Omlin, N. Tunariu, G. Boysen, N. Porta, P. Flohr, A. Gillman, I. Figueiredo, C. Paulding, G. Seed, S. Jain, C. Ralph, A. Protheroe, S. Hussain, R. Jones, T. Elliott, U. McGovern, D. Bianchini, J. Goodall, Z. Zafeiriou, C.T. Williamson, R. Ferraldeschi, R. Riisnaes, B. Ebbs, G. Fowler, D. Roda, W. Yuan, Y.-M. Wu, X. Cao, R. Brough, H. Pemberton, R. A'Hern, A. Swain, L.P. Kunju, R. Eeles, G. Attard, C.J. Lord, A. Ashworth, M.A. Rubin, K.E. Knudsen, F.Y. Feng, A.M. Chinnaiyan, E. Hall, and J.S. de Bono

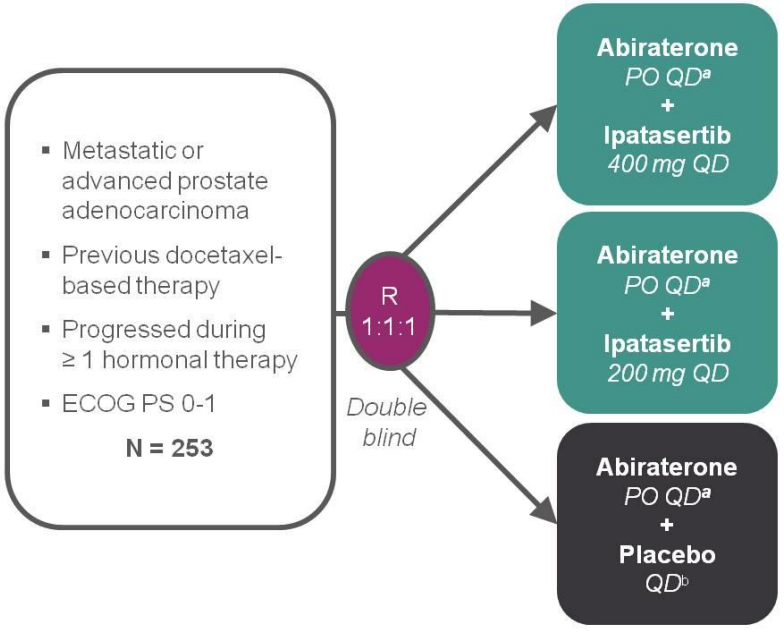
TOPARP-A



Background

A.MARTIN Phase II trial design

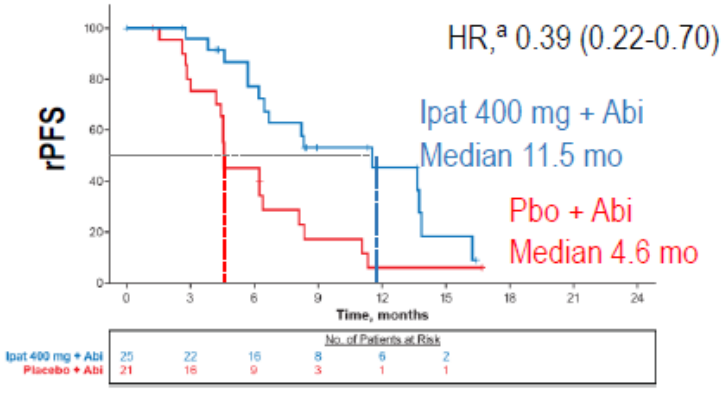
- This Phase II study evaluated the Akt inhibitor ipatasertib in combination with the anti-androgen abiraterone in patients with mCRPC
- Patients were stratified accordingly:
  - Enzalutamide (yes or no)
  - Number of chemotherapy regimens (1 vs > 1)
  - Progression (PSA only vs other)
- Co-primary efficacy endpoints were rPFS in the all-comer population and in patients whose tumors had PTEN loss
- Secondary endpoints included safety, OS, time to PSA progression and PSA response rate



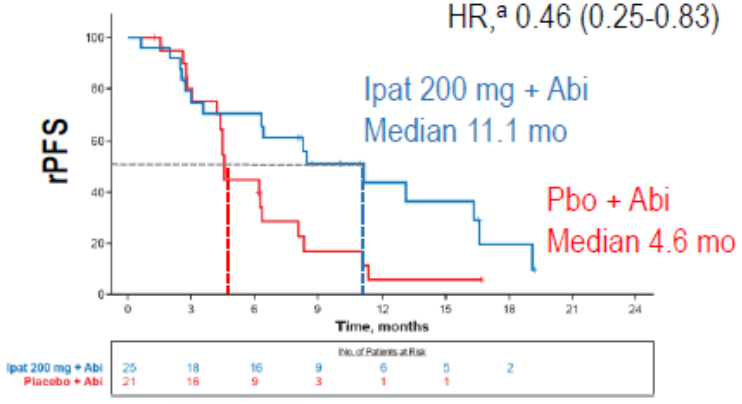
NCT01485861.
ECOG PS, Eastern Cooperative Oncology Group performance score; mCRPC, metastatic castration-resistant prostate carcinoma; OS, overall survival; PO, by mouth; PSA, prostate-specific antigen; PTEN; phosphatase and tensin homolog; QD, daily; rPFS, radiographic progression-free survival.
[a] Abiraterone 1000 mg with prednisone/prednisolone 5 mg twice daily.
[b] Further randomized 1:1 ratio to ipatasertib 400 mg QD/placebo and 200 mg QD/placebo arms.

PTEN Loss

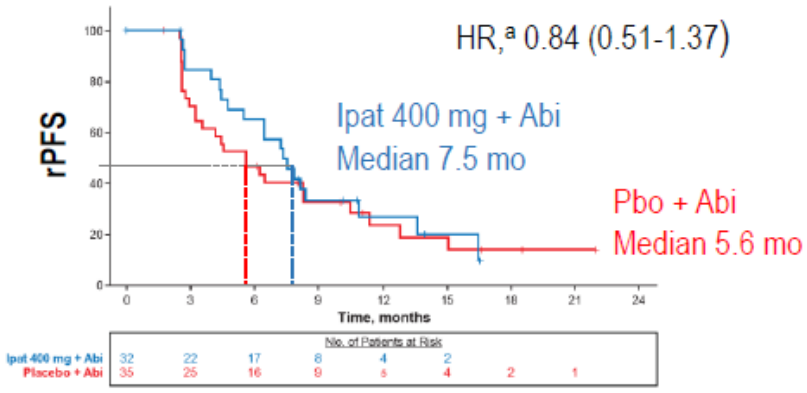
Ipatasertib 400 mg

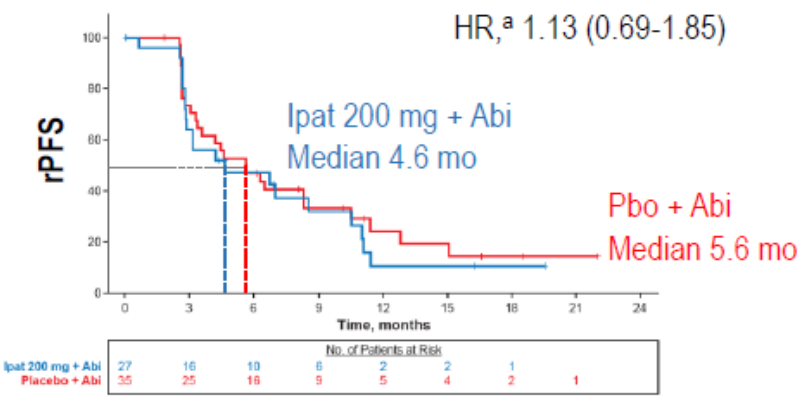


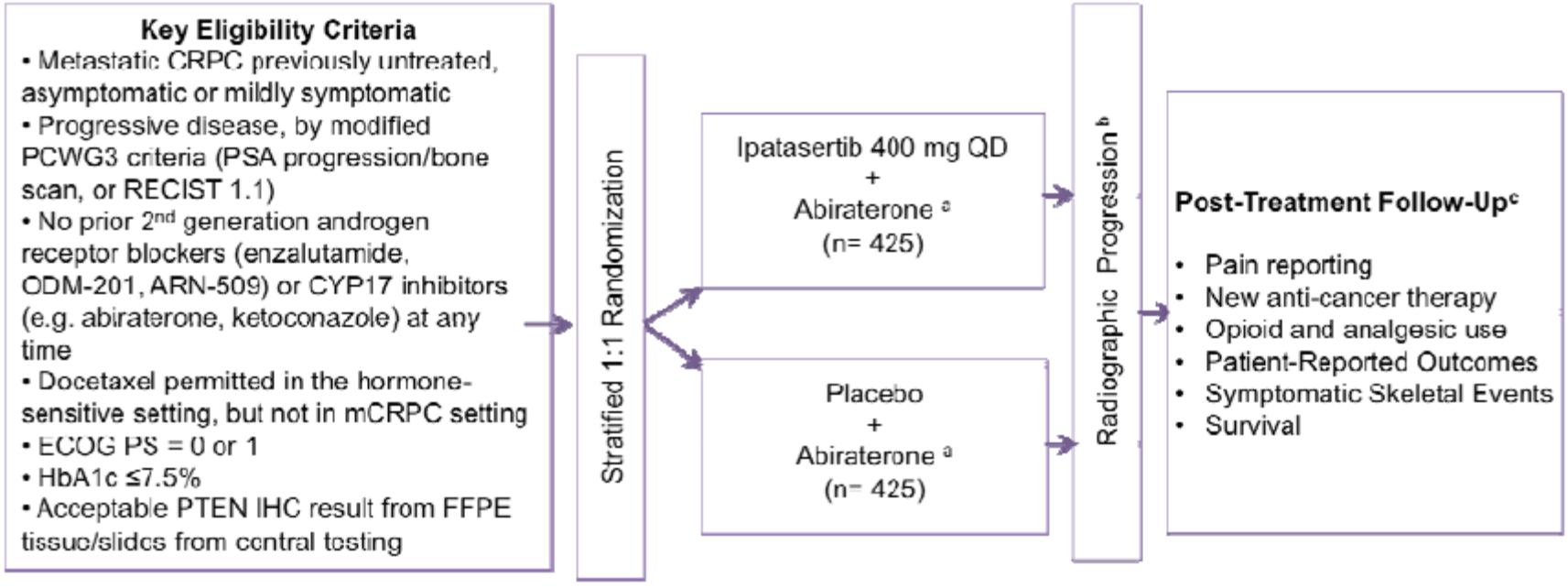
Ipatasertib 200 mg



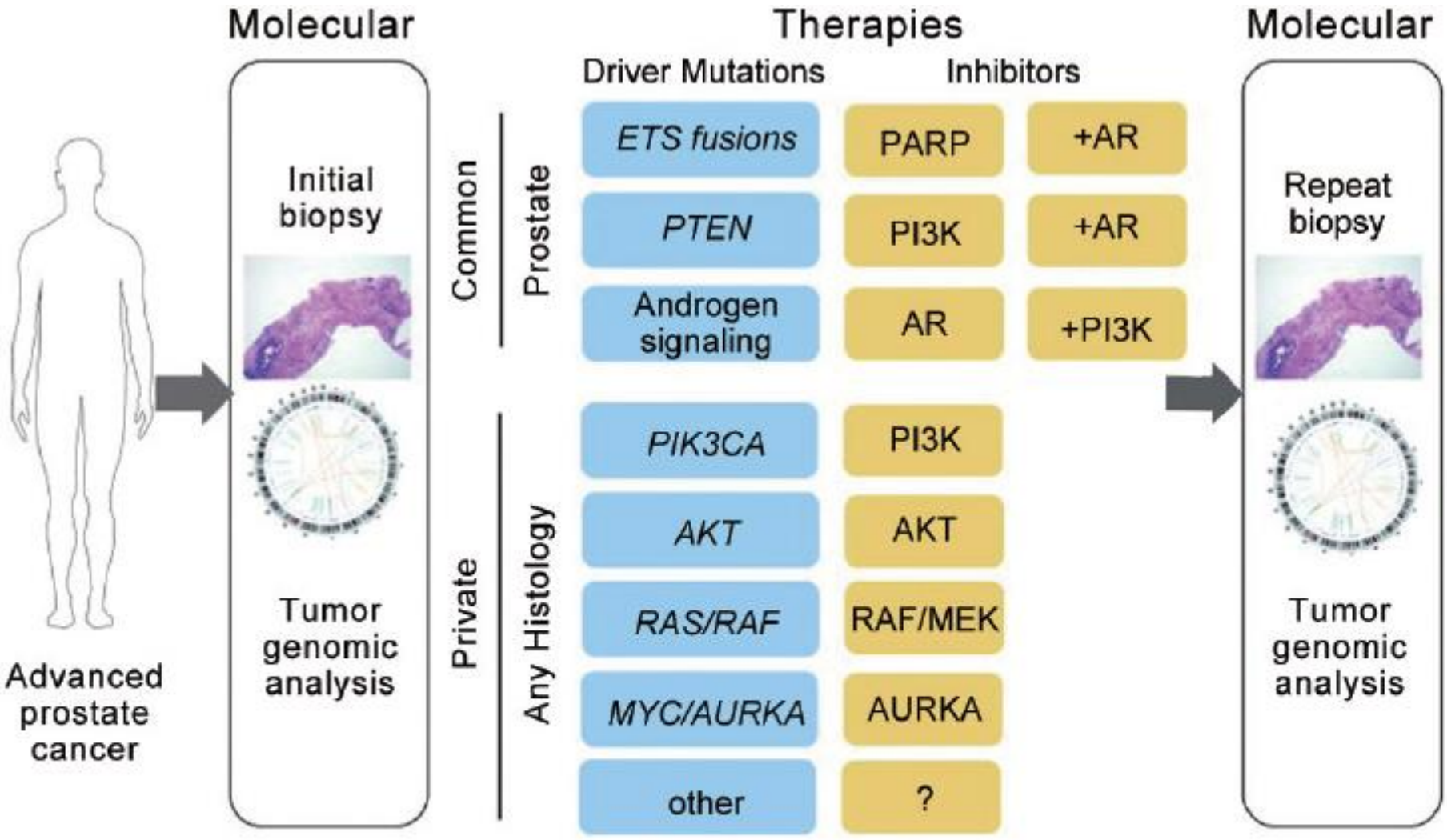
PTEN Non-Loss



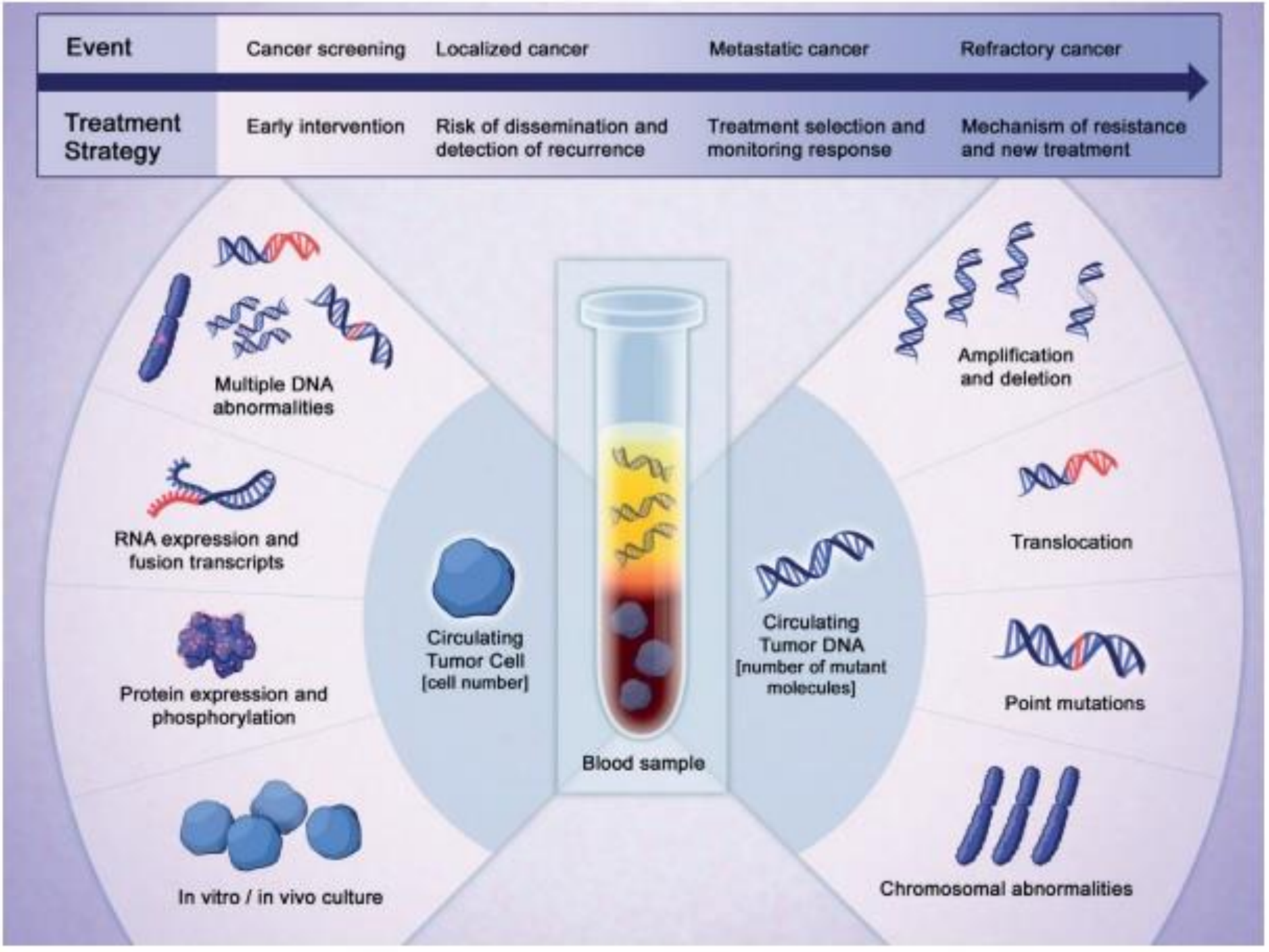


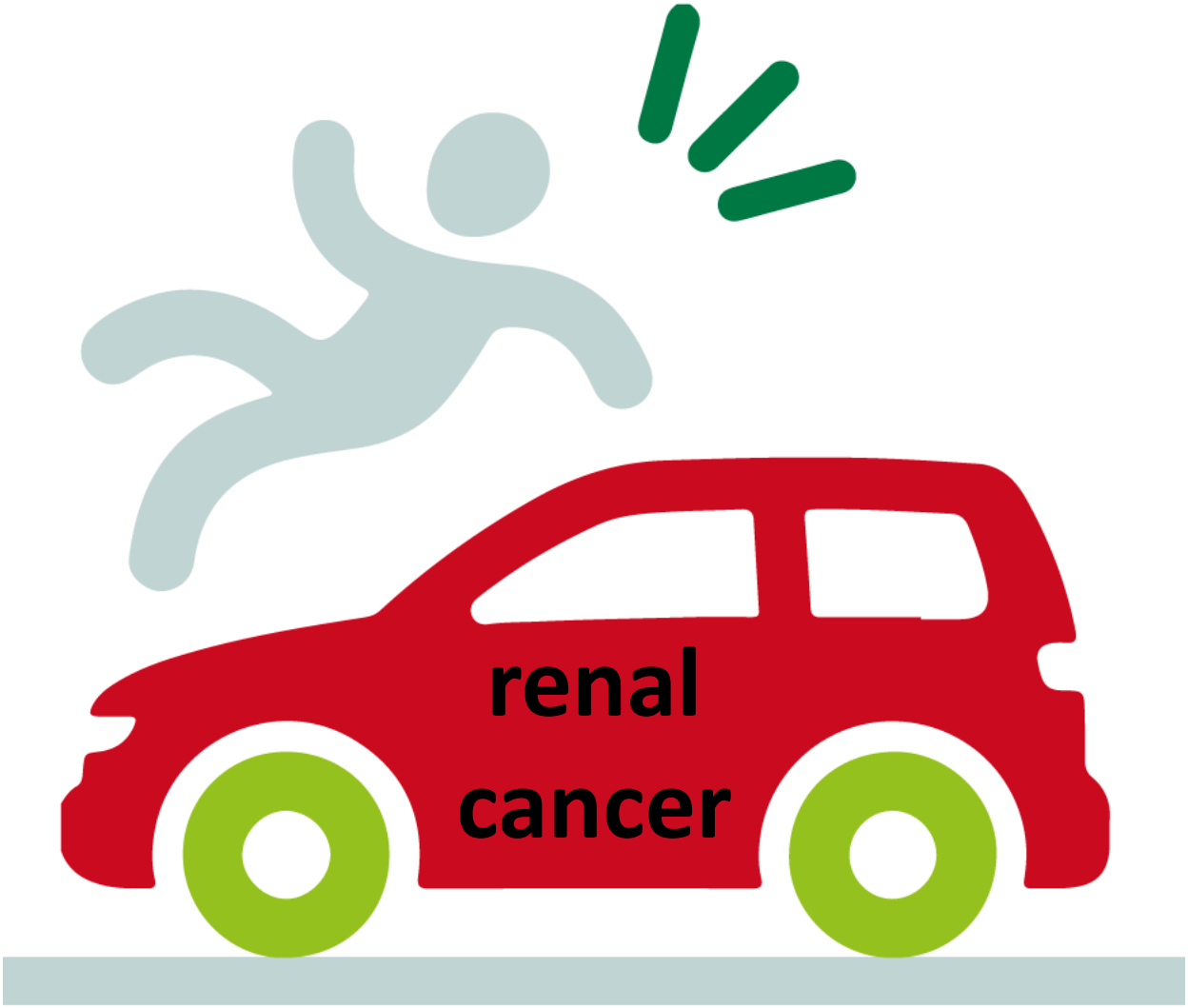

Key Eligibility Criteria
• Metastatic CRPC previously untreated, asymptomatic or mildly symptomatic
• Progressive disease, by modified PCWG3 criteria (PSA progression/bone scan, or RECIST 1.1)
• No prior 2nd generation androgen receptor blockers (enzalutamide, ODM-201, ARN-509) or CYP17 inhibitors (e.g. abiraterone, ketoconazole) at any time
• Docetaxel permitted in the hormone-sensitive setting, but not in mCRPC setting
• ECOG PS = 0 or 1
• HbA1c ≤7.5%
• Acceptable PTEN IHC result from FFPE tissue/slides from central testing
Stratified 1:1 Randomization
Ipatasertib 400 mg QD
+
Abiraterone a
(n= 425)
Placebo
+
Abiraterone a
(n= 425)
Radiographic Progression b
Post-Treatment Follow-Up c
• Pain reporting
• New anti-cancer therapy
• Opioid and analgesic use
• Patient-Reported Outcomes
• Symptomatic Skeletal Events
• Survival

tomorrow the challenge will be the availability of biological samples



From Shevrin Asian J Androl 18: 586-591

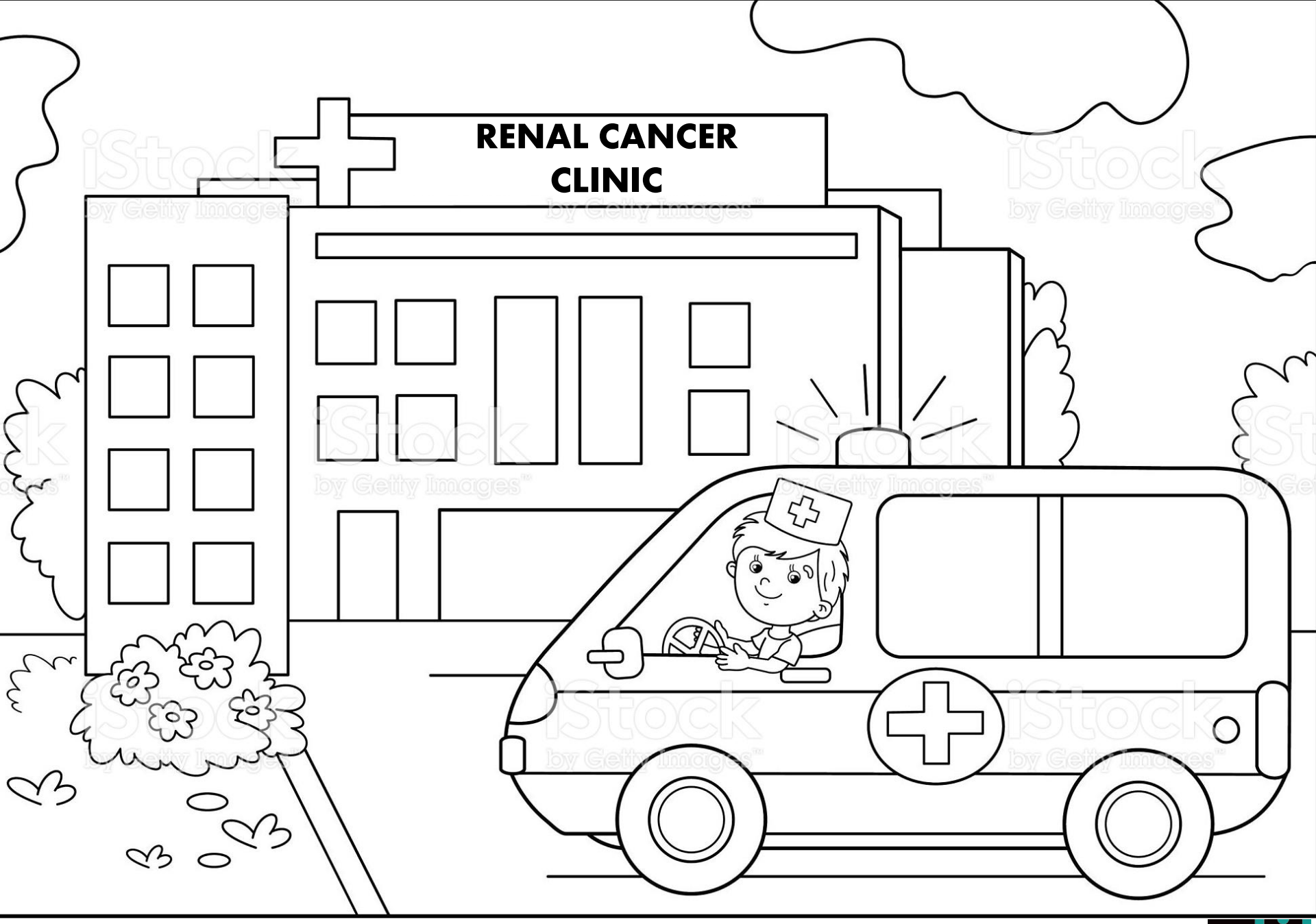

Event
Cancer screening
Localized cancer
Metastatic cancer
Refractory cancer
Treatment Strategy
Early intervention
Risk of dissemination and detection of recurrence
Treatment selection and monitoring response
Mechanism of resistance and new treatment
Multiple DNA abnormalities
RNA expression and fusion transcripts
Protein expression and phosphorylation
In vitro / in vivo culture
Circulating Tumor Cell [cell number]
Blood sample
Circulating Tumor DNA [number of mutant molecules]
Amplification and deletion
Translocation
Point mutations
Chromosomal abnormalities



XVIII CONGRESSO
DI ONCOLOGIA TREVIGLIESE

Un incidente
di percorso

Unità Operativa
di Oncologia Medica
Ospedale di Trento


RENAL CANCER
CLINIC

The dark age (before 2005)

17009 (2017) Hsieh et al modified

Table 1 High-Dose Interleukin-2 (IL-2) in Advanced Renal Cell Carcinoma

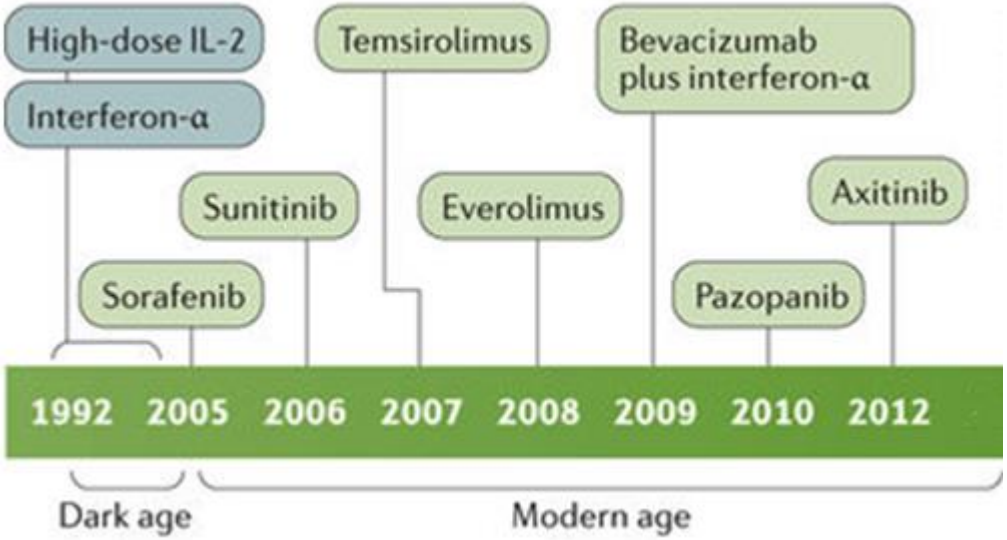
Study	N	Dose	Overall Response Rate	Response Duration
7 Phase II studies[10]	255	600,000–720,000 IU/kg	15% CR = 7% PR = 8%	Overall median: 54 mos (3 to 131+) Median in CRs: 80+ mos (7 to 131+) Median in PRs: 20 mos (3 to 126+)
Randomized phase II (two-arm)[21]	155	720,000 IU/kg	21% (CR = 11, PR = 22)	8/11 ongoing CRs at 9.3 yrs
	149	72,000 IU/kg	13% (CR = 6, PR = 13)	3/6 ongoing CRs at 10.1 yrs
Randomized phase II (three-arm)[21]	96	720,000 IU/kg	21%	8/11 ongoing CRs at 9.3 yrs
	93	72,000 IU/kg	11%	3/6 ongoing CRs at 10.1 yrs
	94	SQ low-dose	10%	1 CR, 78+ mos
Phase III[11]	91	SQ low-dose IL2 + IFN	10% (CR = 3)	15 mos
	95	600,000 IU/kg	23% (CR = 8)	24 mos
NCI experience (single institution)[12]	259	720,000 IU/kg	20% (CR = 23, PR = 30)	In 21 pts with CR, median survival not reached at 221+ mos
Phase II "SELECT" study[65]	120	600,000 IU/kg	29%	20 responders (4 to 35+ mos)
LCI experience (single institution)[a]	104	720,000 IU/kg	26% (CR = 8, PR = 19)	5/8 CRs: ongoing response at 122+ mos 2/19 PRs: ongoing response at 84+ mos

[a]White RL, Amin A, et al (unpublished data).
CR = complete response; IFN = interferon; LCI = Levine Cancer Institute; NCI = National Cancer Institute; PR = partial response; SQ = subcutaneous.

The dark age (before 2005)

17009 (2017) Hsieh et al modified

The modern age (2005-2014)

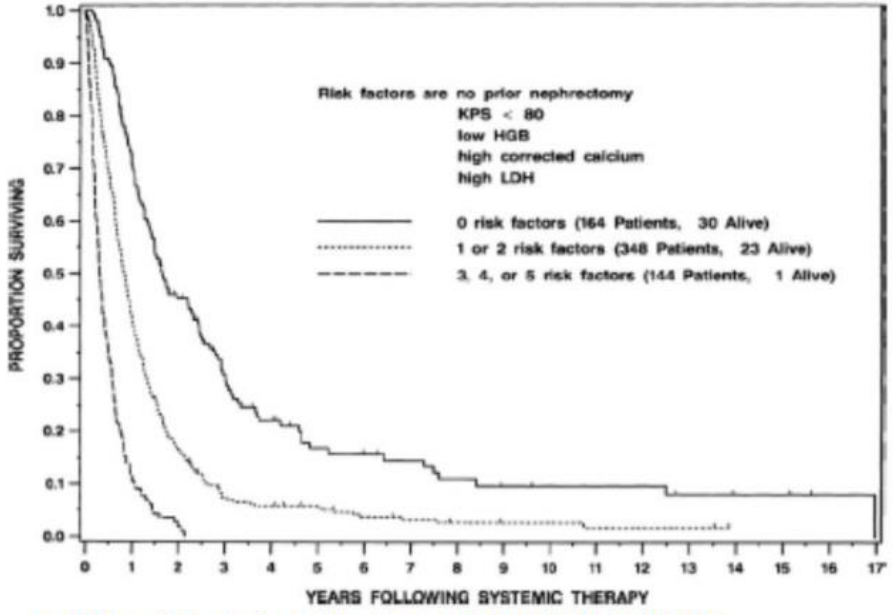


nature REVIEWS DISEASE PRIMERS

17009 (2017) Hsieh et al modified

Well established algorithm

Regimen	Setting	Therapy	Options
Treatment Naïve Patient	MSK Risk : Good or Intermediate	Sunitinib Bevacizumab ± IFNα Pazopanib	HD IL-2 ? Sorafenib
	MSK Risk : Poor	Temsirolimus Sunitinib	?Sorafenib
Treatment Refractory Patient (≥ 2nd Line)	Cytokine Refractory	Sorafenib Pazopanib	Sunitinib
	Refractory to VEGF/ VEGFR or mTOR Inhibitors	Everolimus Axitinib	?Sequential TKI's or VEGFInhibitor



1. Motzer RJ, et al. *J Clin Oncol.* 1999;17(8):2530-2540.

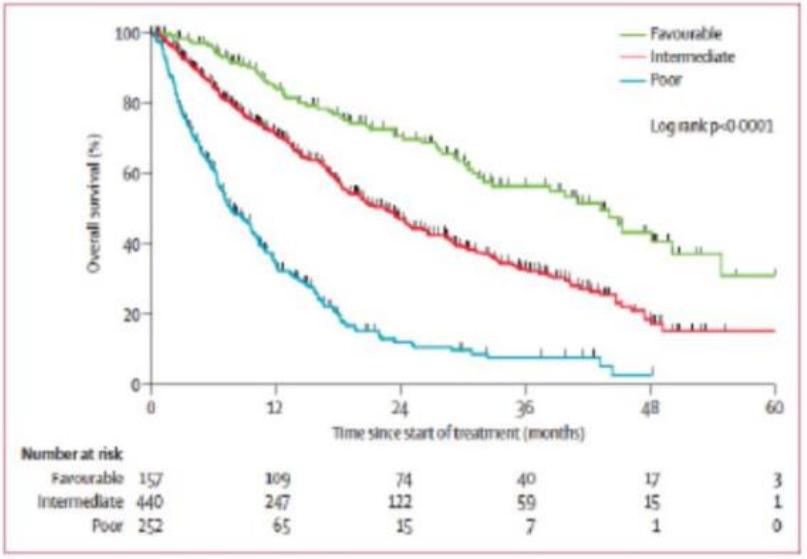
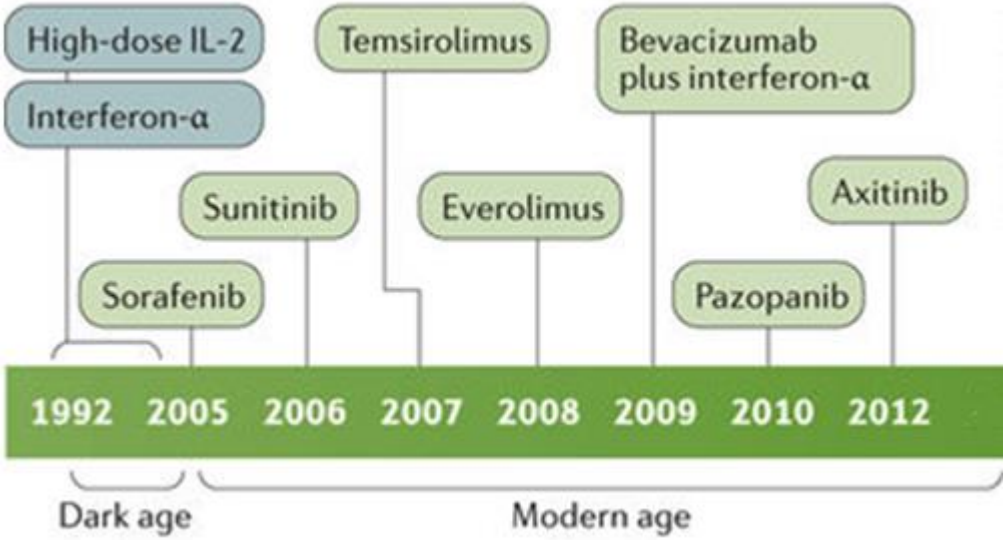


Figure 1: Results of Kaplan-Meier analysis of overall survival for the Database Consortium model

2. Heng DY, et al. *Lancet Oncol.* 2013;14(2):141-148.

	Pre–Targeted Agents Era[1]	Targeted Agents Era[2]
Median OS of good-risk patients	20 months	43.2 months (95% CI: 31.4–50.1)
Median OS of intermediate-risk patients	10 months	22.5 months (95% CI: 18.7–25.1)
Median OS of poor-risk patients	4 months	7.8 months (95% CI: 6.5–9.7)

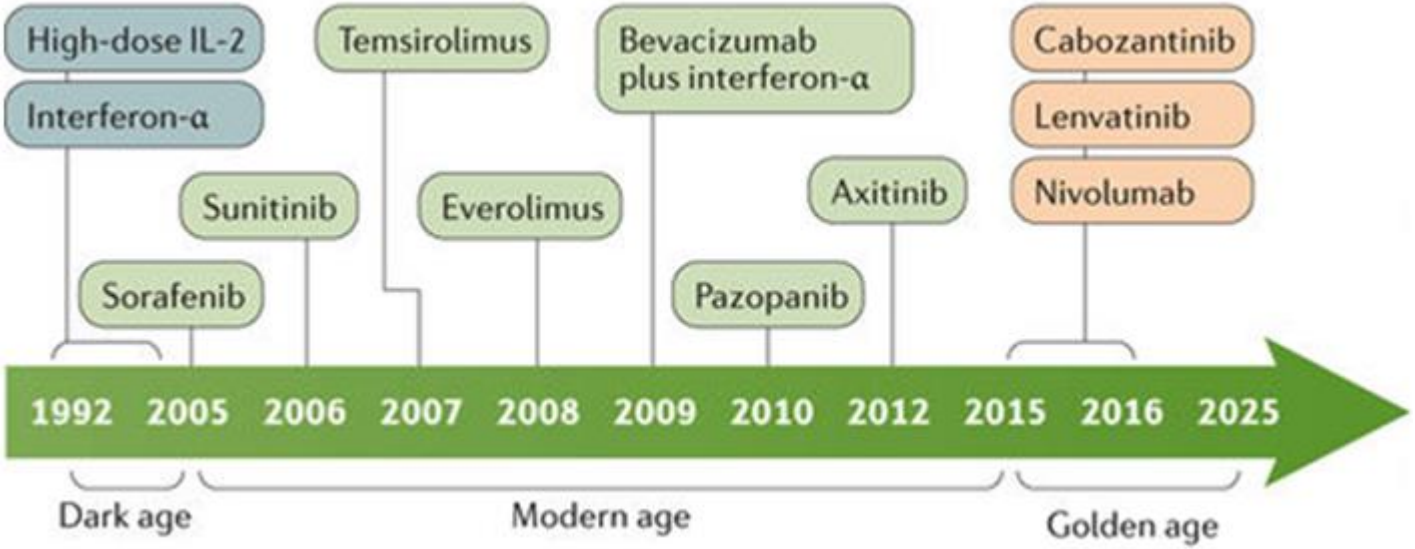
The modern age (2005-2014)



nature REVIEWS DISEASE PRIMERS

17009 (2017) Hsieh et al modified

The gold age (after 2014)



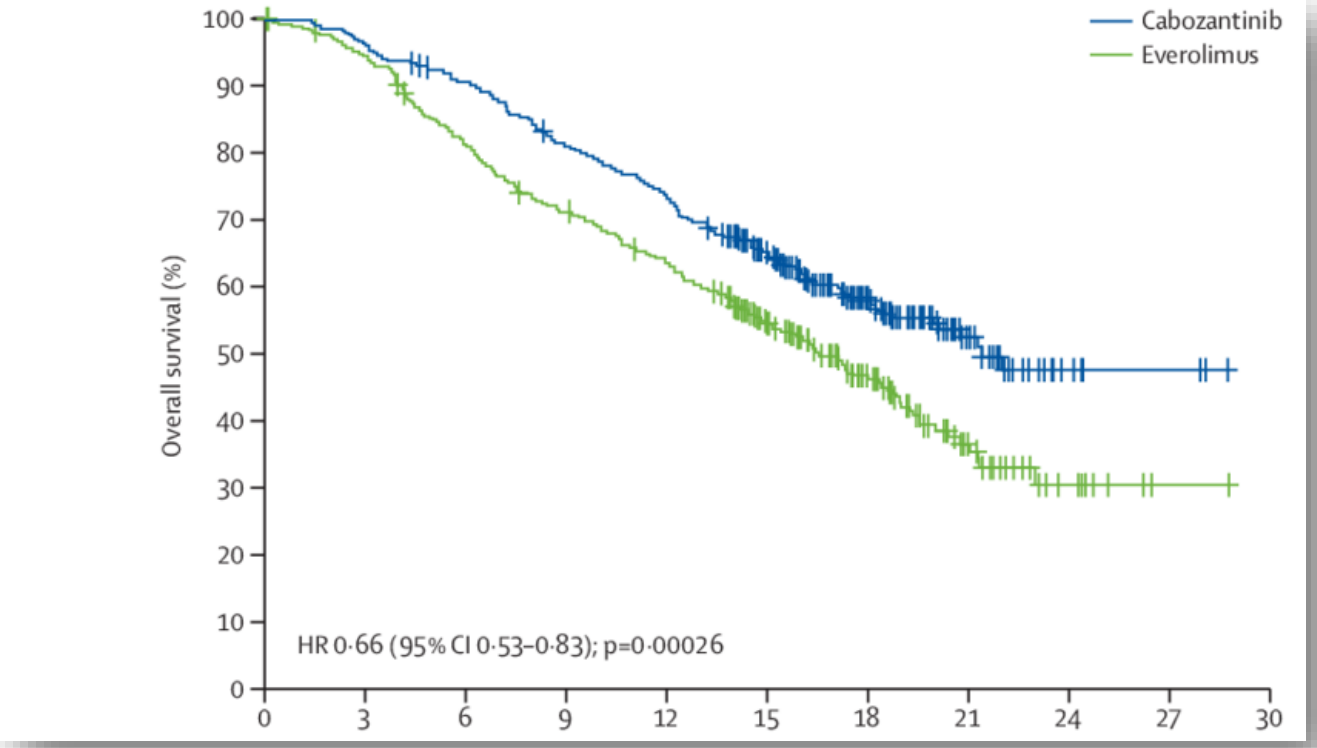
17009 (2017) Hsieh et al modified

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N ENGL J MED 373;19 NEJM.ORG NOVEMBER 5, 2015

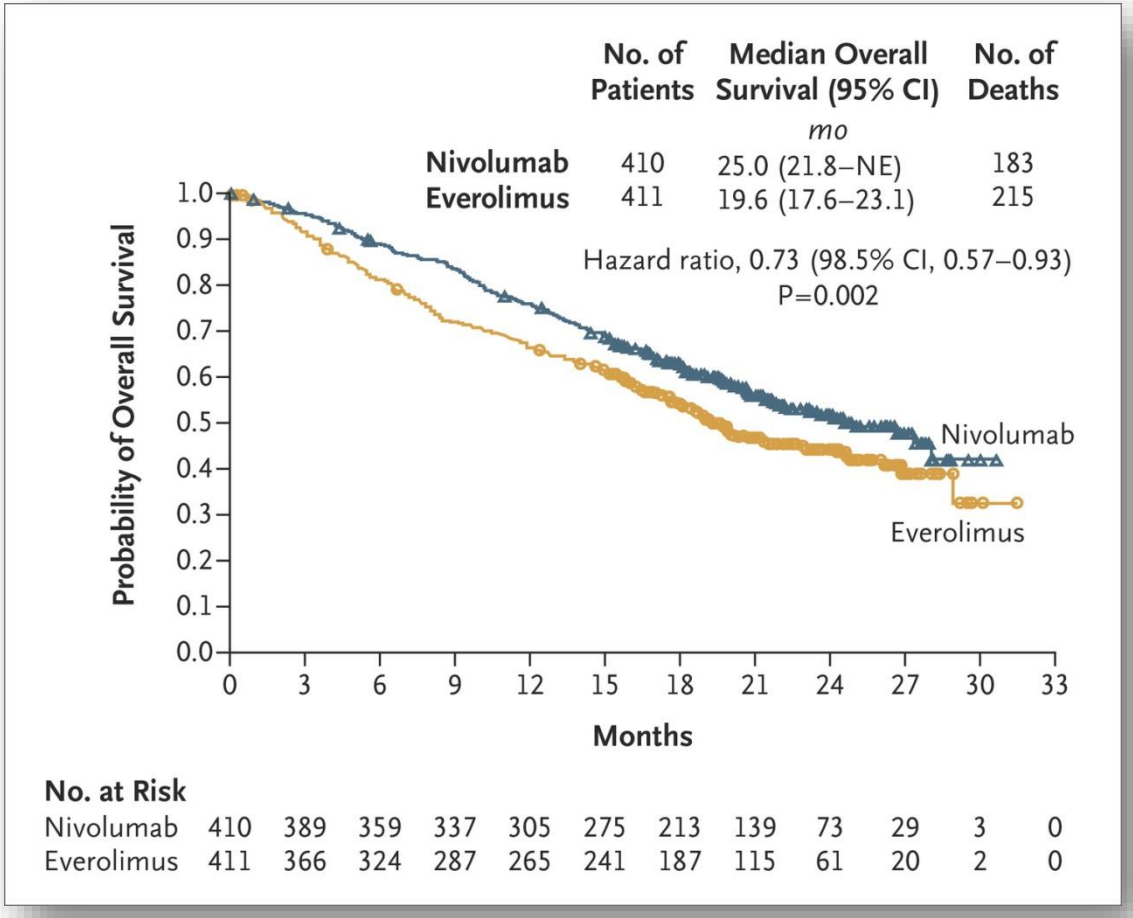
Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 5, 2015 VOL. 373 NO. 19

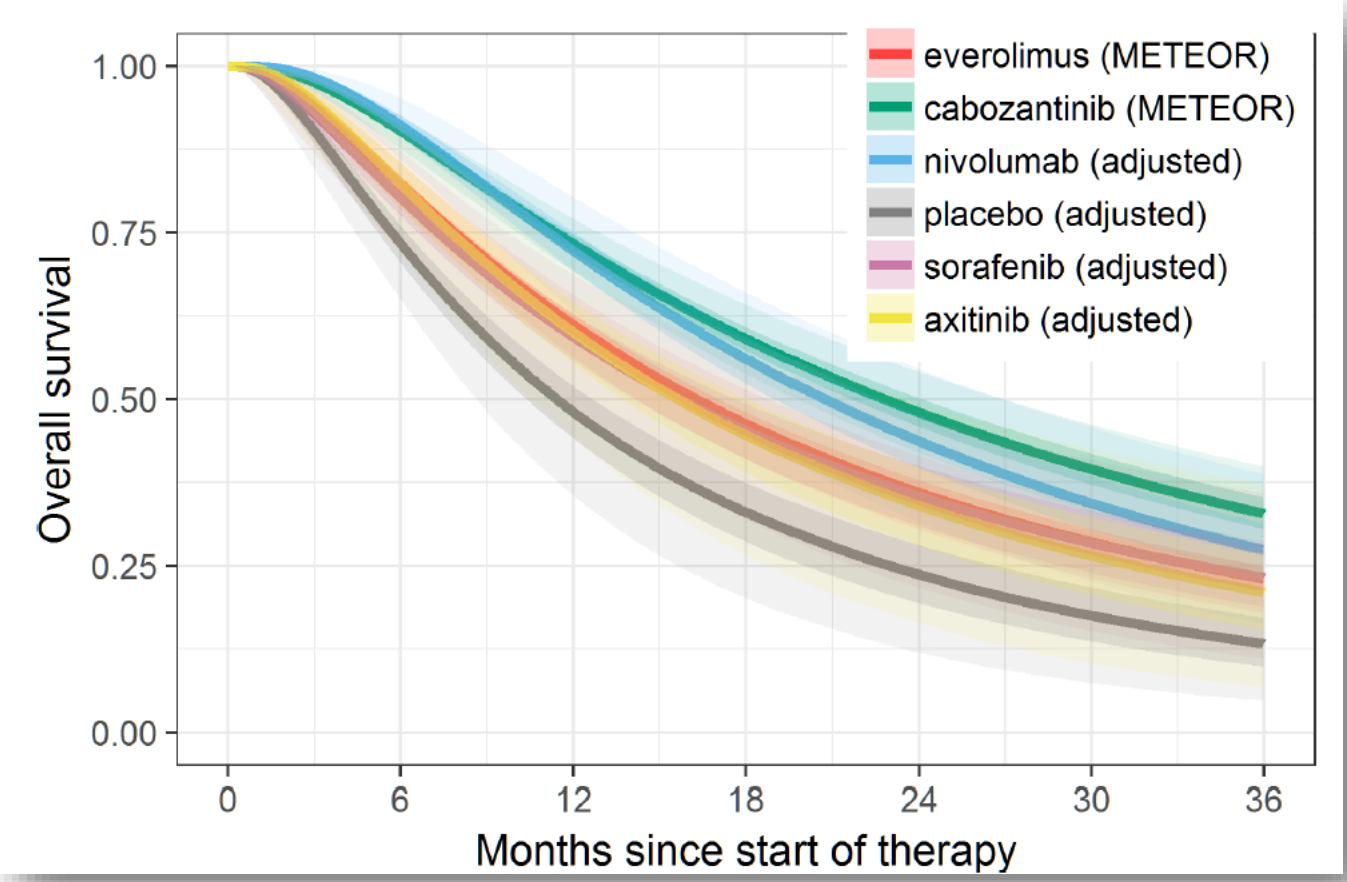
Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma



PLOS ONE

Cabozantinib versus everolimus, nivolumab, axitinib, sorafenib and best supportive care: A network meta-analysis of progression-free survival and overall survival in second line treatment of advanced renal cell carcinoma

12(9): e0184423.



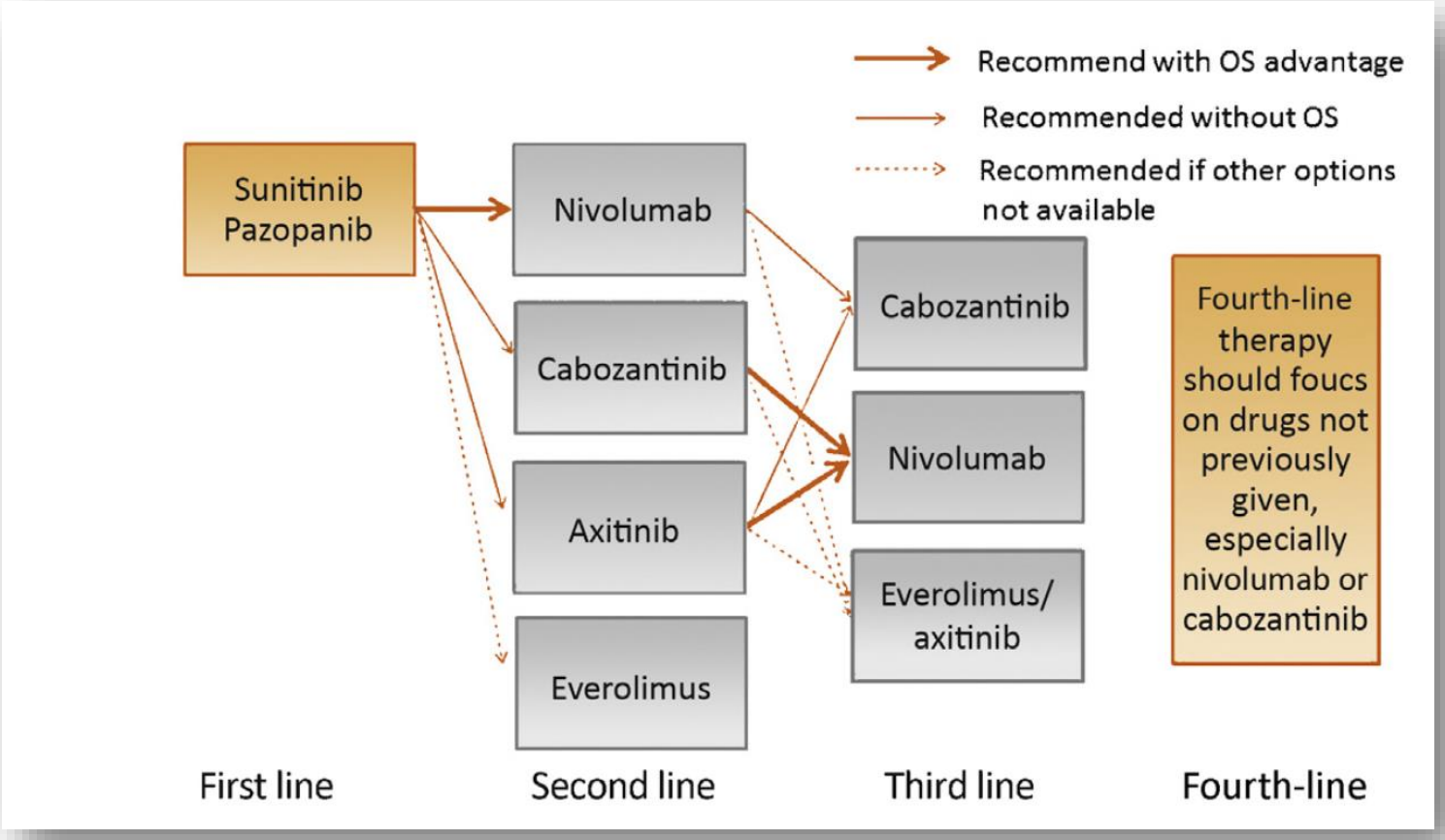
EUROPEAN UROLOGY 69 (2016) 4–6

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

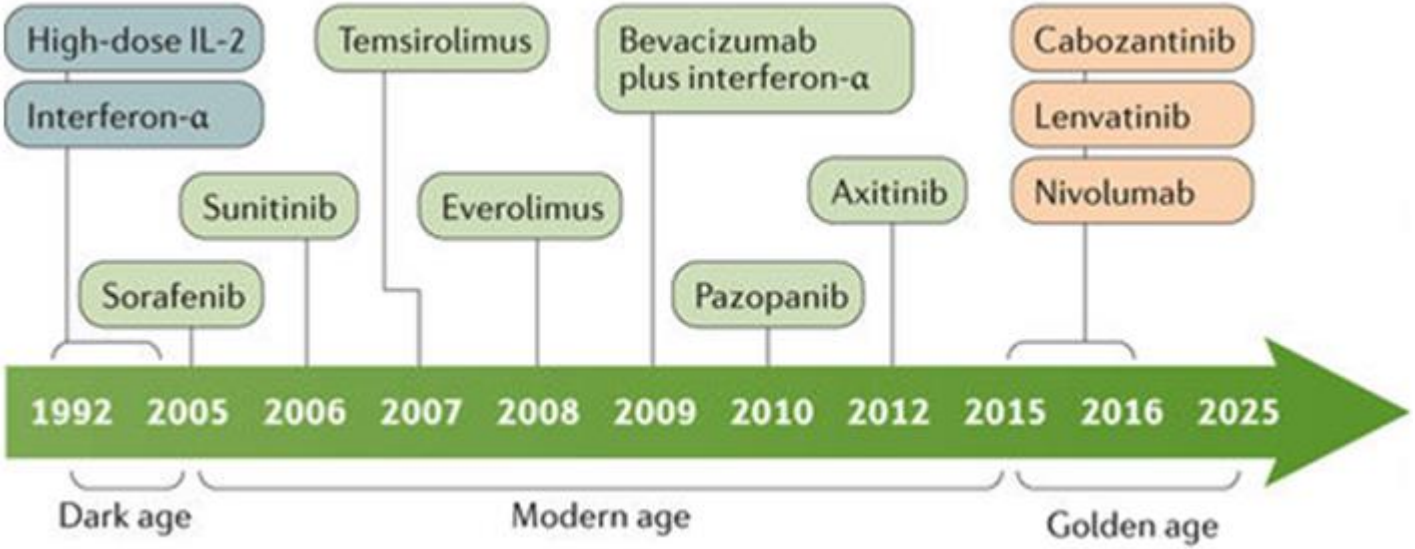
European Association of Urology

Platinum Opinion

Updated EAU Guidelines for Clear Cell Renal Cancer Patients Who Fail VEGF Targeted Therapy

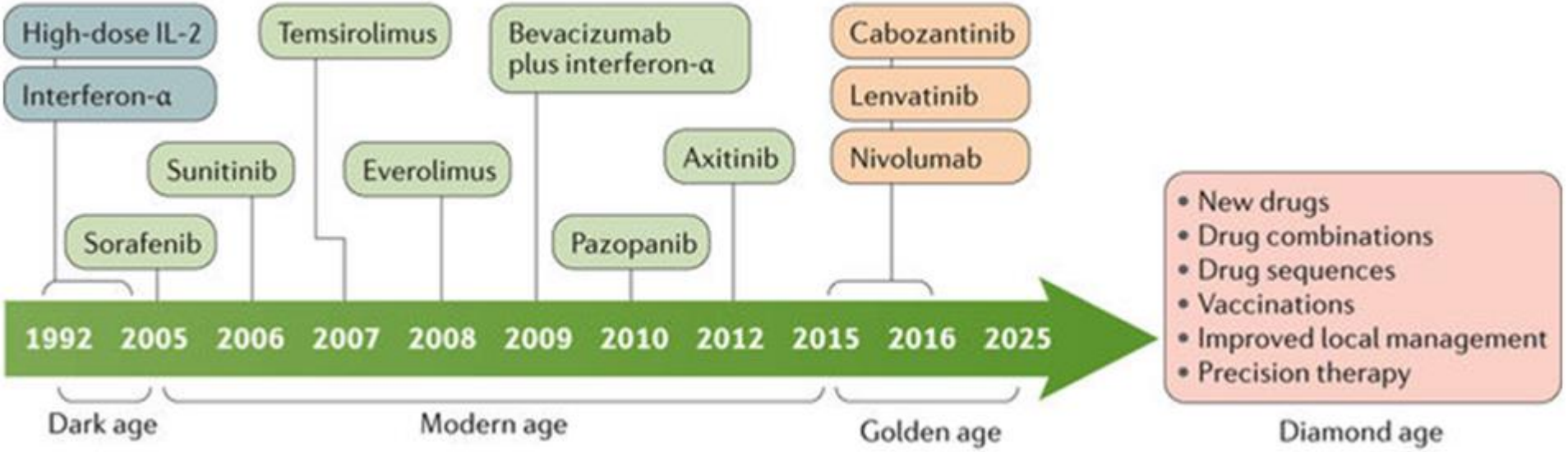


The gold age (after 2014)



17009 (2017) Hsieh et al modified

The diamond age (after 2025)



nature REVIEWS DISEASE PRIMERS

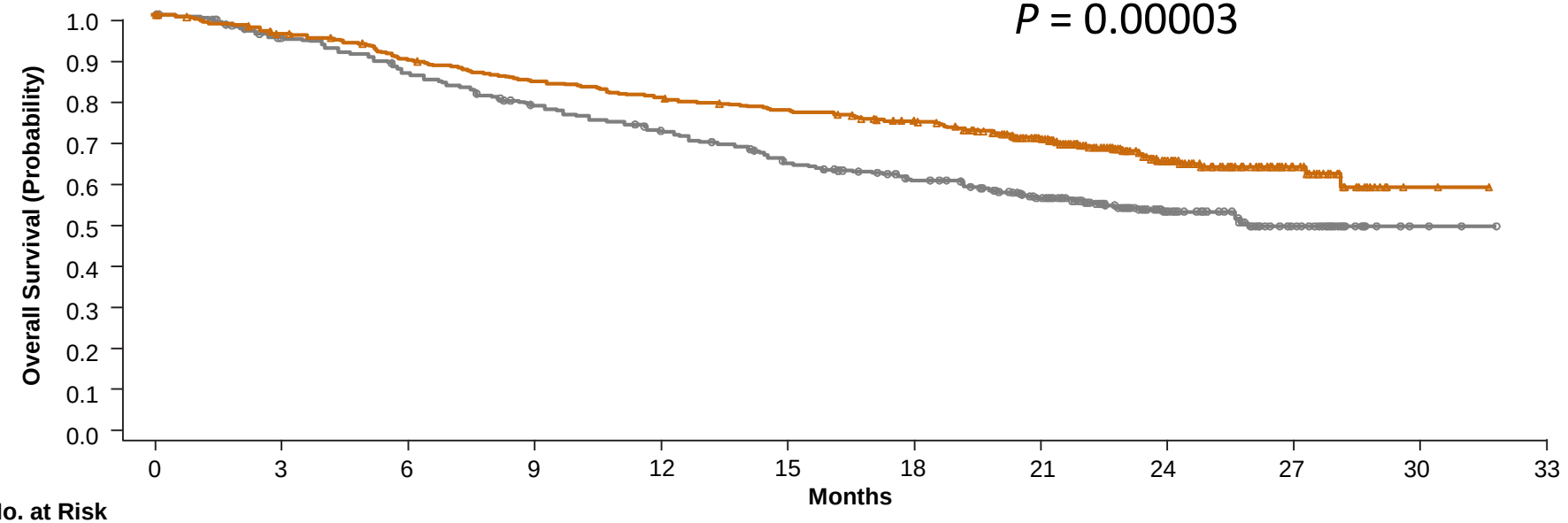
17009 (2017) Hsieh et al modified

OS per IRC in IMDC intermediate/poor risk pts

Median OS, months (95% CI)	
NIVO + IPI	NR (28.2–NE)
SUN	26.0 (22.1–NE)

Hazard ratio (99.8% CI), 0.63 (0.44–0.89)

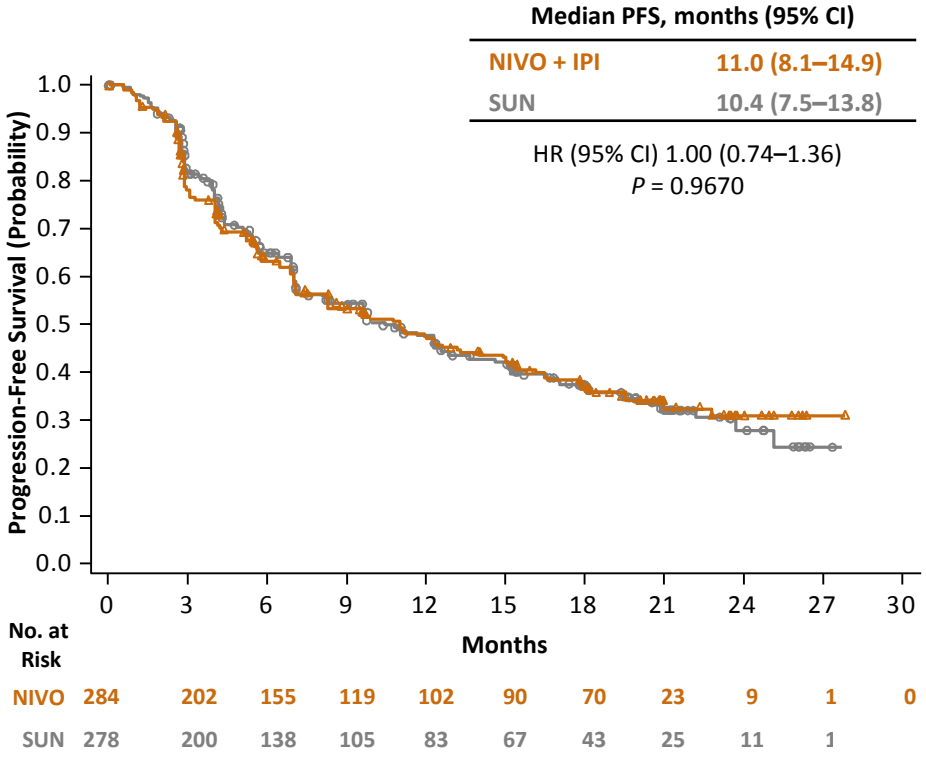
P = 0.00003



No. at Risk												
NIVO + IPI	425	399	372	348	332	318	300	241	119	44	2	0
SUN	422	387	352	315	288	253	225	179	89	34	3	0

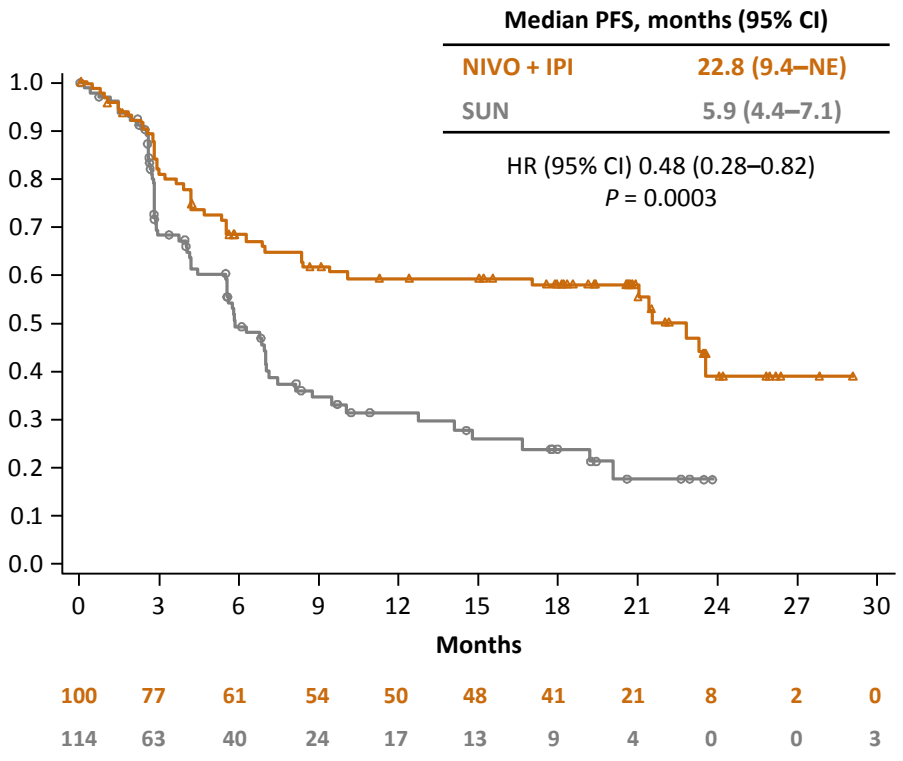
Exploratory endpoints: activity by PD-L1

PD-L1 <1% (n = 562)

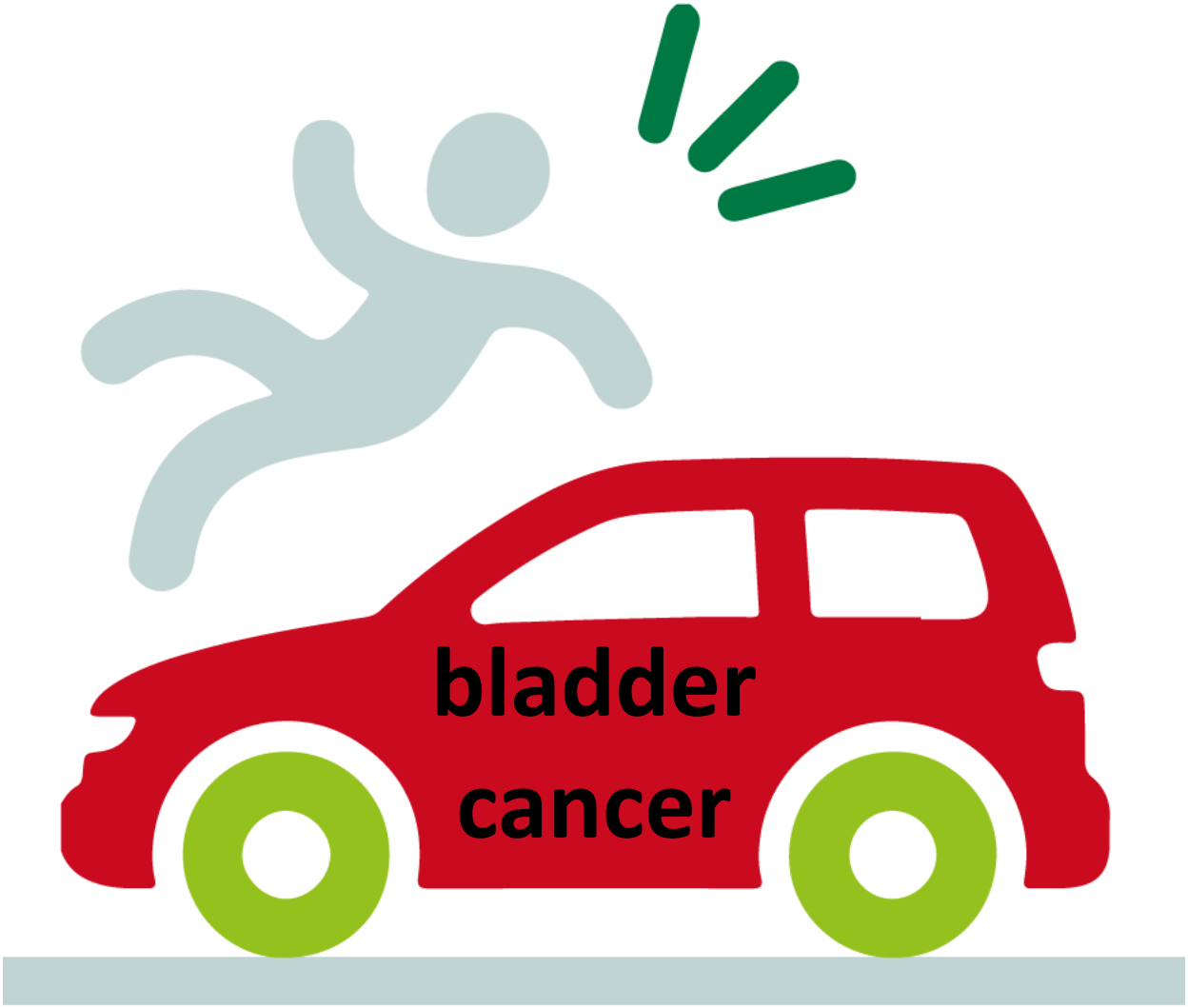


No. at Risk											
NIVO	284	202	155	119	102	90	70	23	9	1	0
SUN	278	200	138	105	83	67	43	25	11	1	

PD-L1 ≥1% (n = 214)

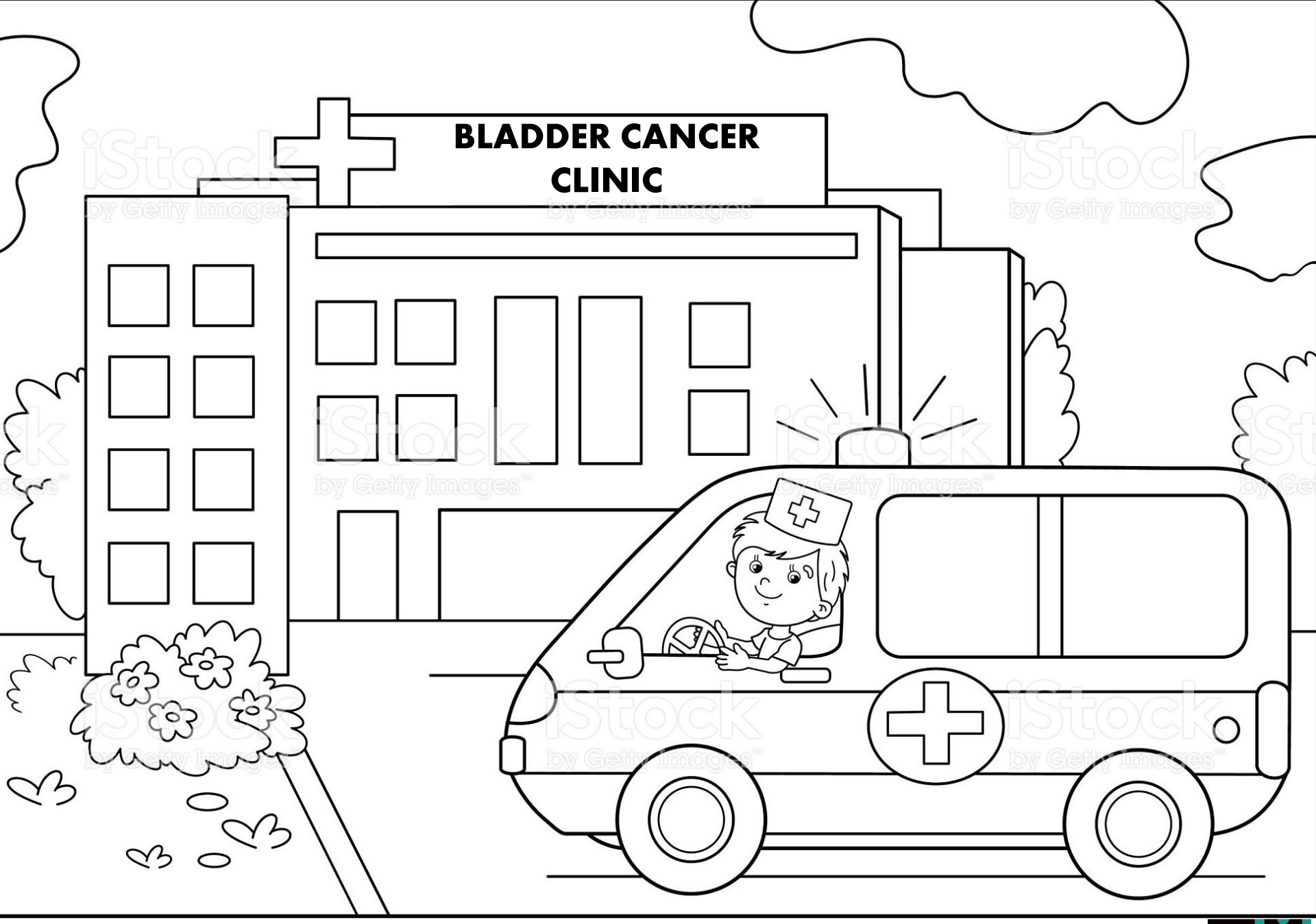


NIVO	100	77	61	54	50	48	41	21	8	2	0
SUN	114	63	40	24	17	13	9	4	0	0	3



XVIII CONGRESSO
DI ONCOLOGIA TREVIGLIESE
Un incidente
di percorso

Unità Operativa
di Oncologia Medica
Ospedale di Trento


BLADDER CANCER
CLINIC

yesterday

	1st line		2nd line
	CDDP-FIT	CDDP-UNFIT	
	MVAC=GC=HD-MVAC ± PACLITAXEL	CBDCA or Vinflunine/GEM CBDCA/GEM or MCaVI Monotherapy	Vinflunine Taxanes or CBDCA
ORR	43-55%	43-50% 30-41% 8-20%	
mPFS	7.6-8.3 mos	5.9-6.1 mos 4.2-5.8 mos 2.4-4.9 mos	
mOS	12.7-15.8 mos	12.8-14 mos 8.3-9.3 mos 5.5-9.0 mos	6.9 mos (vs 4.6 BSC) 6.4

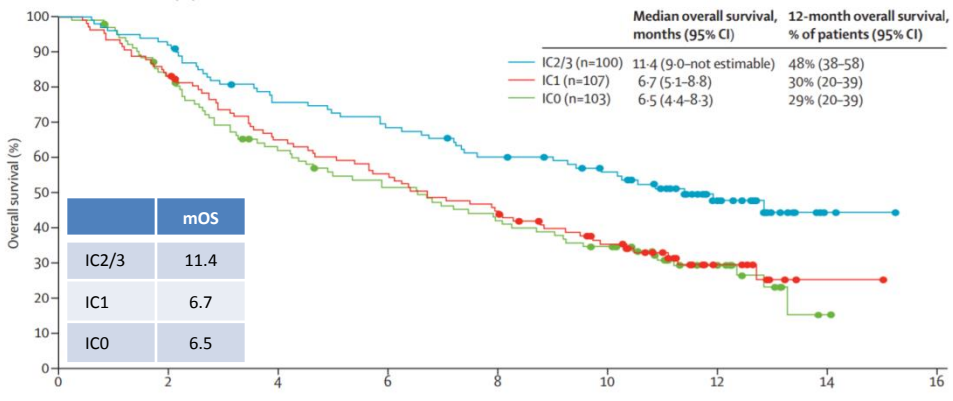
Galsky et al J Clin Oncol 2011

today

Second line

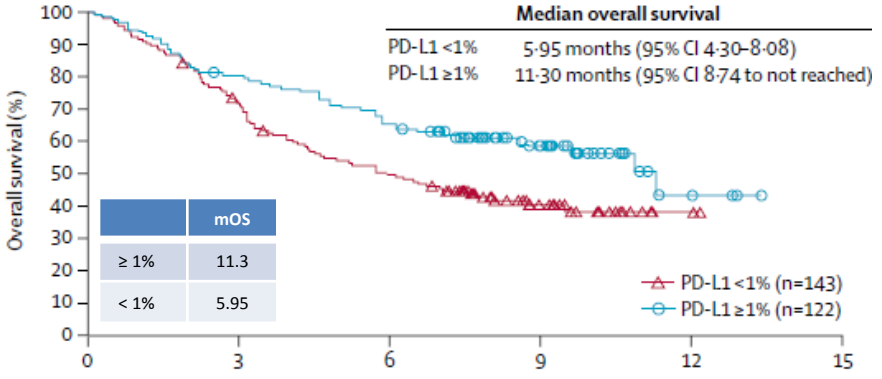
Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, phase 2 trial

Lancet 2016; 387: 1909–20



Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial

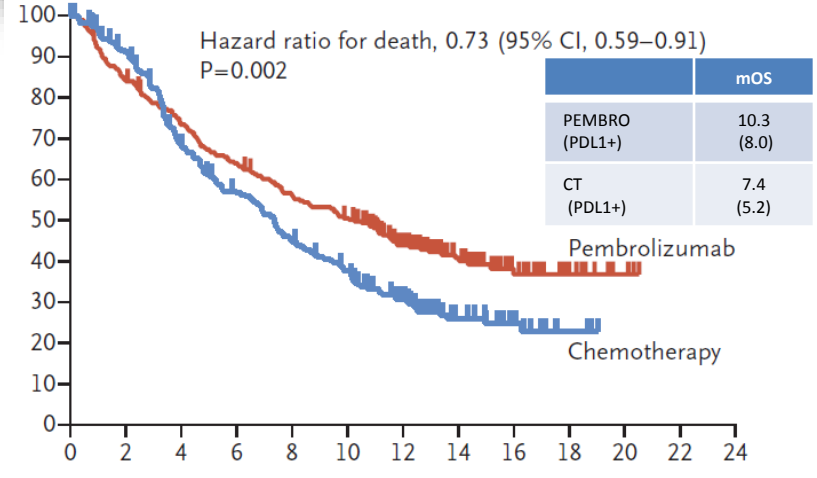
Lancet Oncol 2017; 18: 312–22



The NEW ENGLAND JOURNAL of MEDICINE

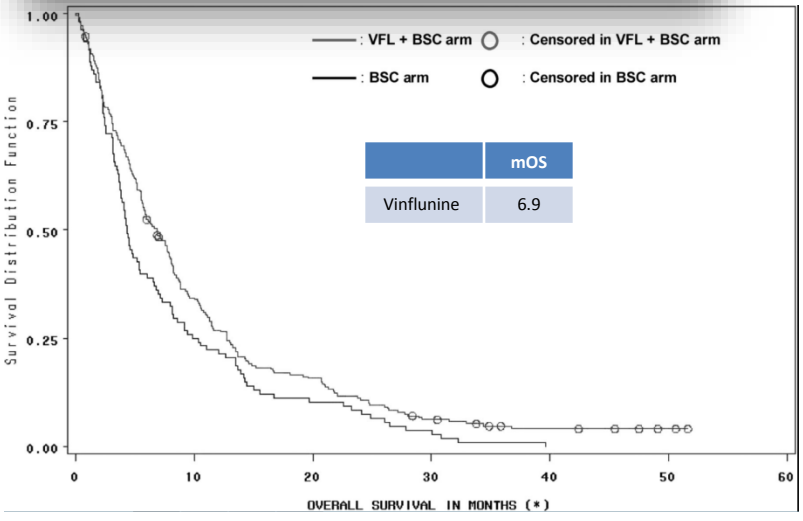
ESTABLISHED IN 1812 MARCH 16, 2017 VOL. 376 NO. 11

Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma



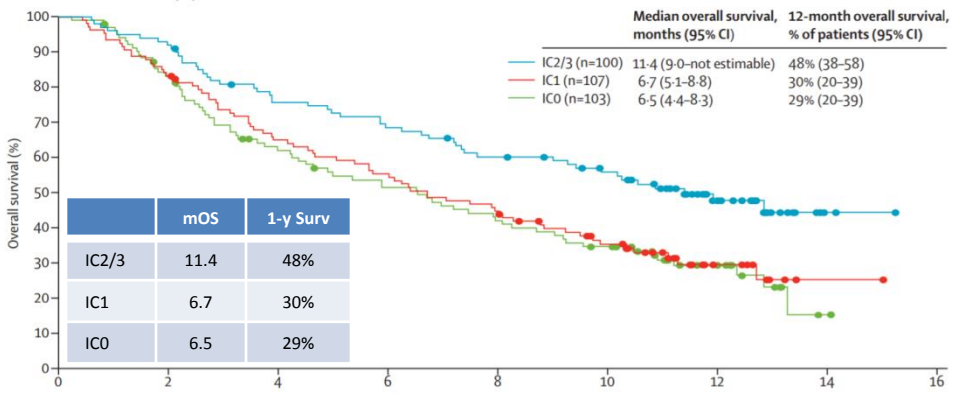
Annals of Oncology 24: 1466–1472, 2013
doi:10.1093/annonc/mdt007
Published online 17 February 2013

Long-term survival results of a randomized phase III trial of vinflunine plus best supportive care versus best supportive care alone in advanced urothelial carcinoma patients after failure of platinum-based chemotherapy†



Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, phase 2 trial

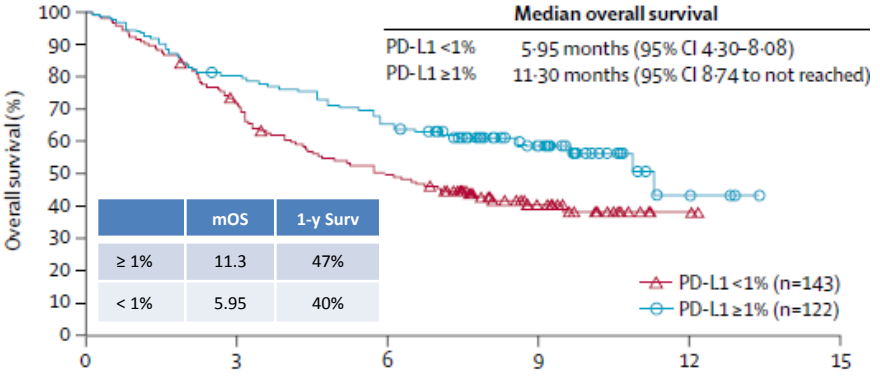
Lancet 2016; 387: 1909–20



	mOS	1-y Surv
IC2/3	11.4	48%
IC1	6.7	30%
IC0	6.5	29%

Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial

Lancet Oncol 2017; 18: 312–22

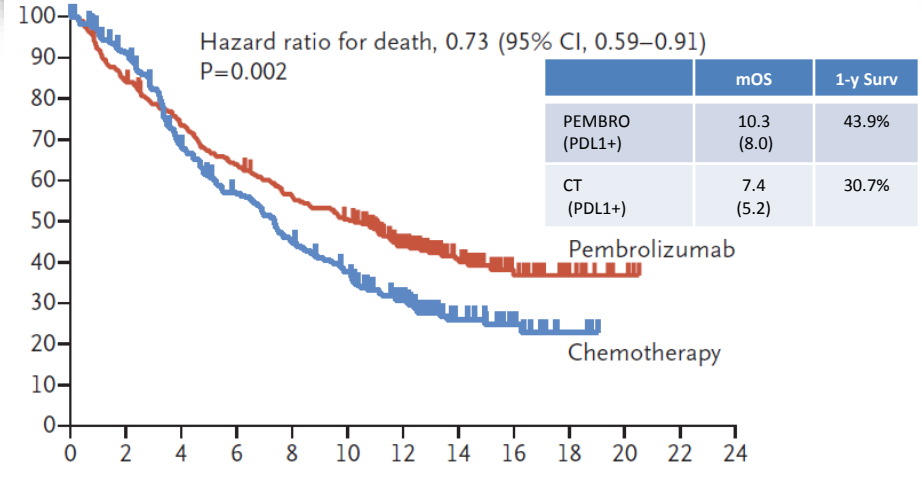


	mOS	1-y Surv
≥ 1%	11.3	47%
< 1%	5.95	40%

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 16, 2017 VOL. 376 NO. 11

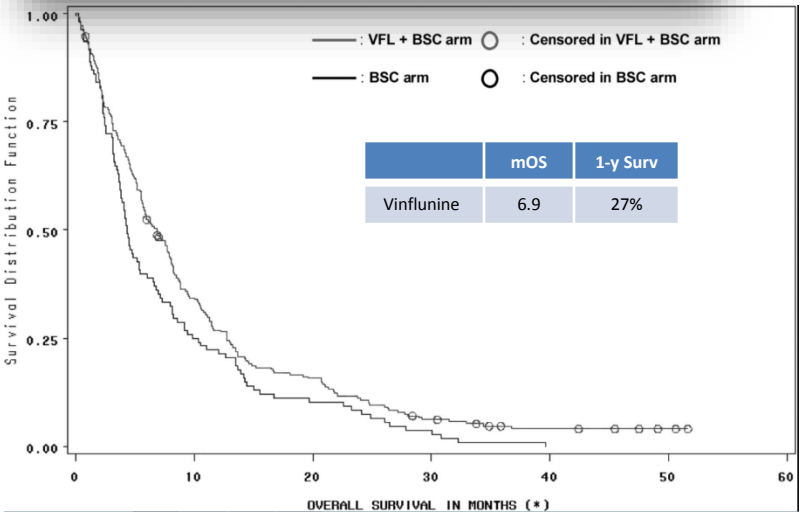
Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma



	mOS	1-y Surv
PEMBRO (PDL1+)	10.3 (8.0)	43.9%
CT (PDL1+)	7.4 (5.2)	30.7%

Annals of Oncology 24: 1466–1472, 2013
doi:10.1093/annonc/mdt007
Published online 17 February 2013

Long-term survival results of a randomized phase III trial of vinflunine plus best supportive care versus best supportive care alone in advanced urothelial carcinoma patients after failure of platinum-based chemotherapy†



	mOS	1-y Surv
Vinflunine	6.9	27%

Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, phase 2 trial

Lancet 2016; 387: 1909–20

- Phase II
- 310 pts
- mFU 11.7 mos

	mOS	1-y Surv
IC2/3	11.4	48%
IC1	6.7	30%
IC0	6.5	29%

Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial

Lancet Oncol 2017; 18: 312–22

- Phase II
- 270 pts
- mFU 7 mos

	mOS	1-y Surv
≥ 1%	11.3	47%
< 1%	5.95	40%

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 16, 2017 VOL. 376 NO. 11

Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma

	mOS	1-y Surv
PEMBRO (PDL1+)	10.3 (8.0)	43.9%
CT (PDL1+)	7.4 (5.2)	30.7%

- Phase III
- 266 pts
- mFU 14.1 mos

Annals of Oncology 24: 1466–1472, 2013
doi:10.1093/annonc/mdt007
Published online 17 February 2013

Long-term survival results of a randomized phase III trial of vinflunine plus best supportive care versus best supportive care alone in advanced urothelial carcinoma patients after failure of platinum-based chemotherapy†

	mOS	1-y Surv
Vinflunine	6.9	27%

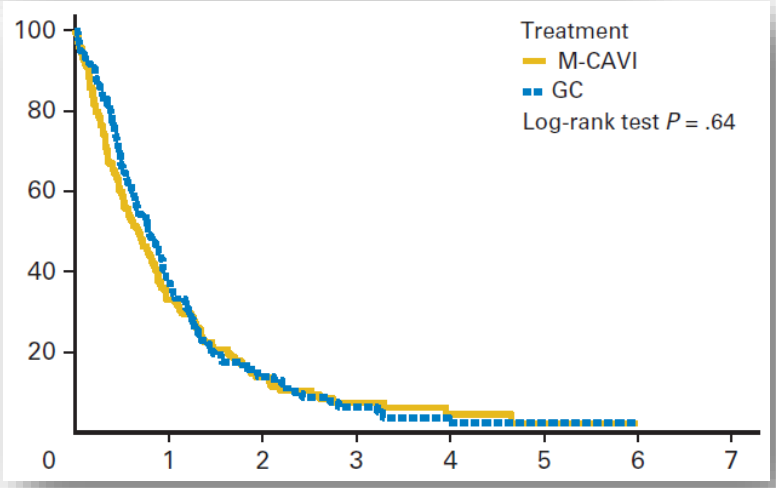
- Phase III
- 253 pts
- mFU 42 mos

today

First line for CDDP-unfit

VOLUME 30 · NUMBER 2 · JANUARY 10 2012
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Randomized Phase II/III Trial Assessing Gemcitabine/Carboplatin and Methotrexate/Carboplatin/ Vinblastine in Patients With Advanced Urothelial Cancer Who Are Unfit for Cisplatin-Based Chemotherapy: EORTC Study 30986

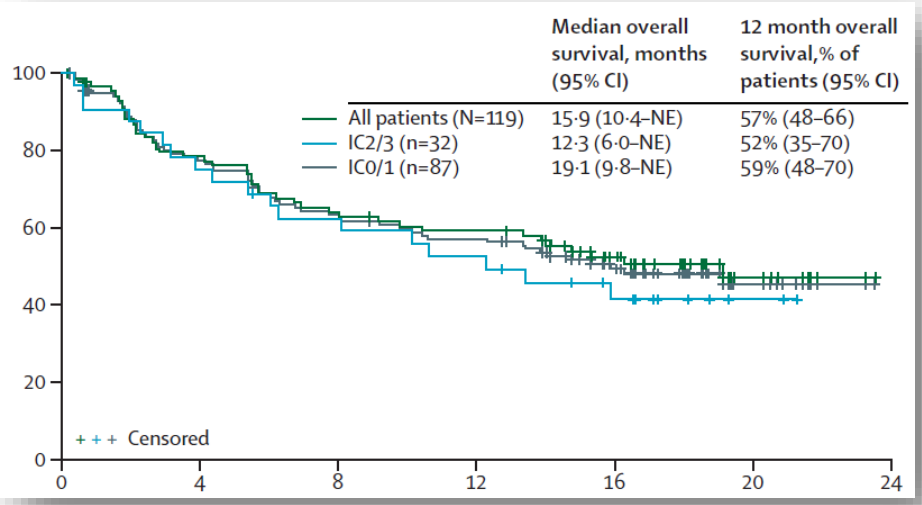


- Phase III
- 118 pts
- mFU 4.5 yrs

- ORR 36%
- mOS 9.3 mos
- 1y Surv Rate 37%

Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm, multicentre, phase 2 trial

Lancet 2017; 389: 67–76



- Phase II
- 119 pts
- mFU 17.2 mos

- ORR 23%
- mOS 15.9 mos
- 1y Surv Rate 57%

today

First line for CDDP-fit

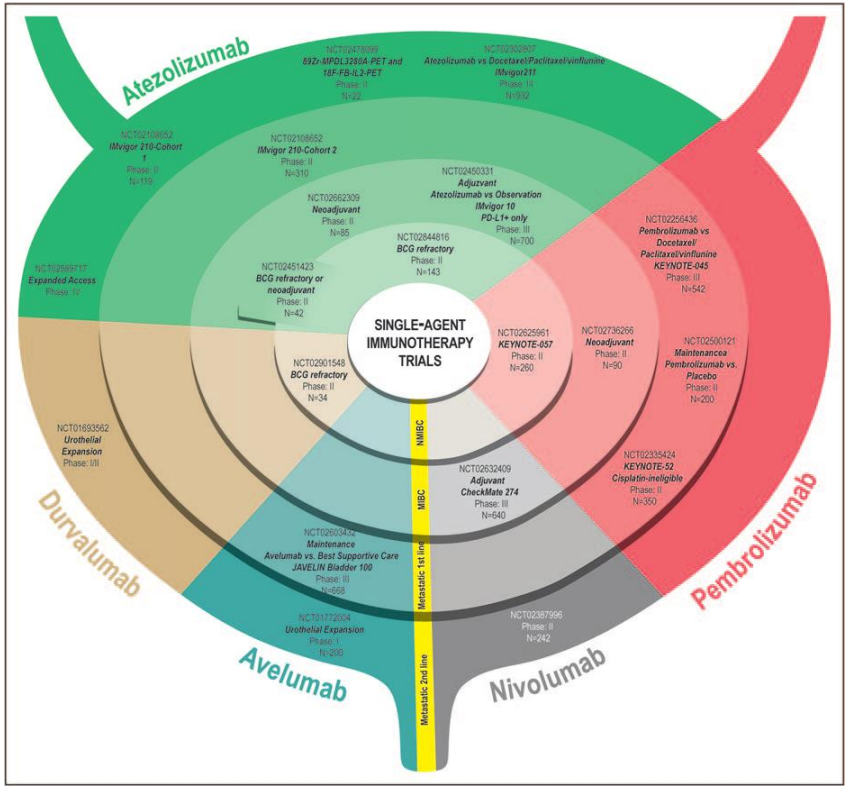
Media Release

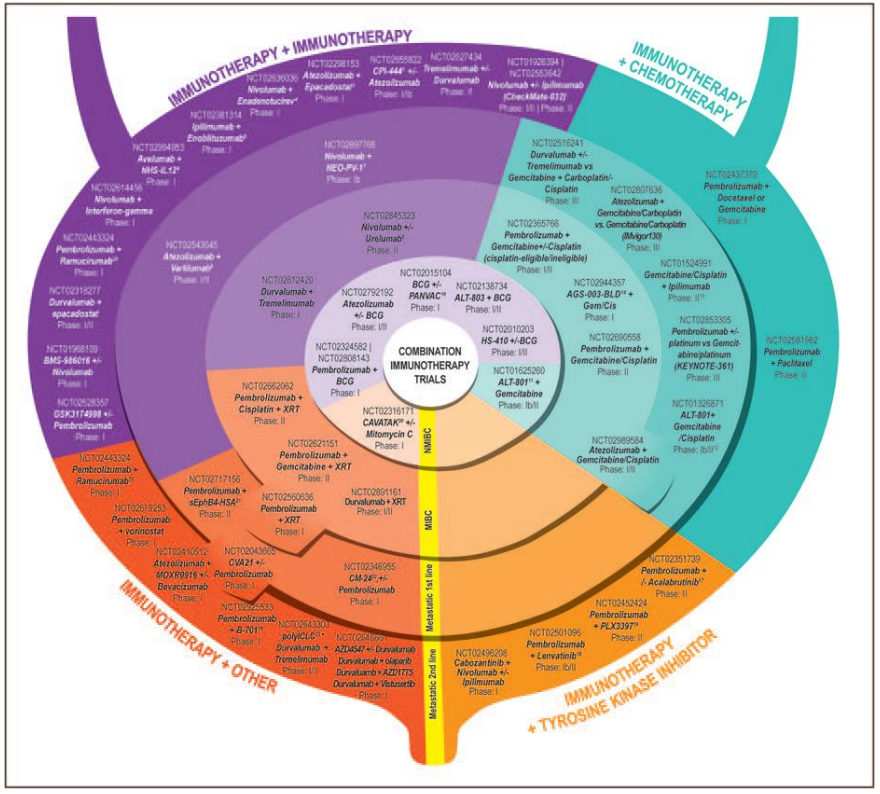
Basel, 10 May 2017

Roche provides update on phase III study of TECENTRIQ® (atezolizumab) in people with previously treated advanced bladder cancer

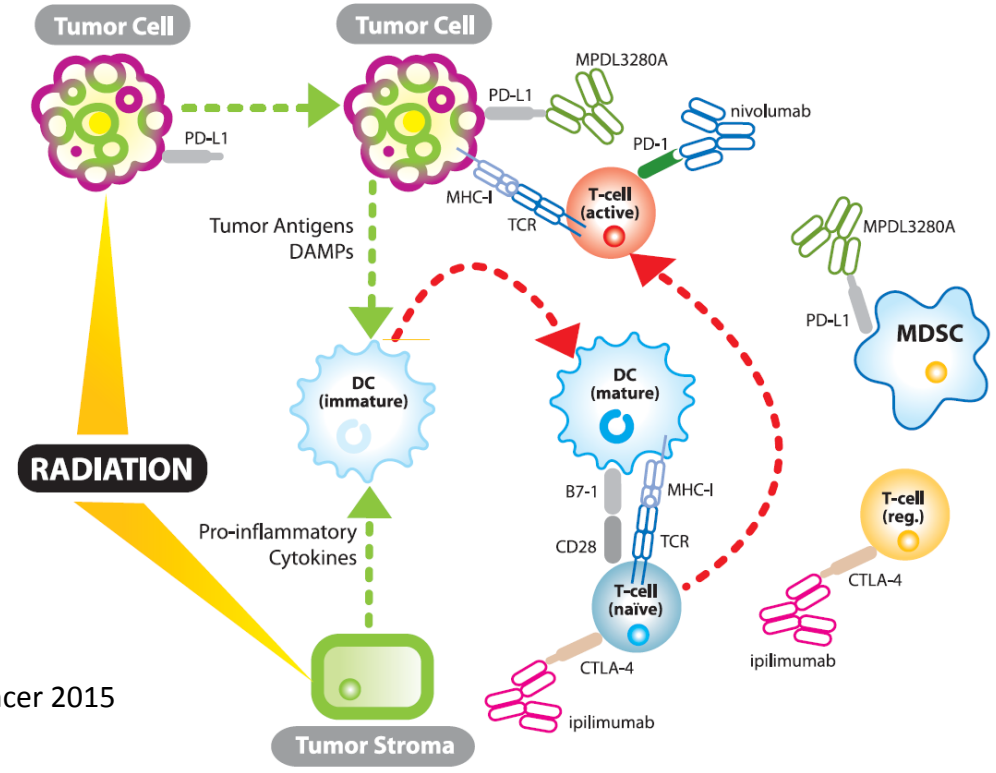
- **IMvigor211 study did not meet its primary endpoint of overall survival (OS) compared to chemotherapy**
- **The safety profile was consistent with what has been previously observed for TECENTRIQ**

tomorrow


Atezolizumab
Durvalumab
Avelumab
Pembrolizumab
Nivolumab
SINGLE-AGENT IMMUNOTHERAPY TRIALS
NMIBC
MIBC
Metastatic 1st line
Metastatic 2nd line


IMMUNOTHERAPY + IMMUNOTHERAPY
IMMUNOTHERAPY + CHEMOTHERAPY
IMMUNOTHERAPY + OTHER
IMMUNOTHERAPY + TYROSINE KINASE INHIBITOR
COMBINATION IMMUNOTHERAPY TRIALS
NMIBC
MIBC
Metastatic 1st line
Metastatic 2nd line

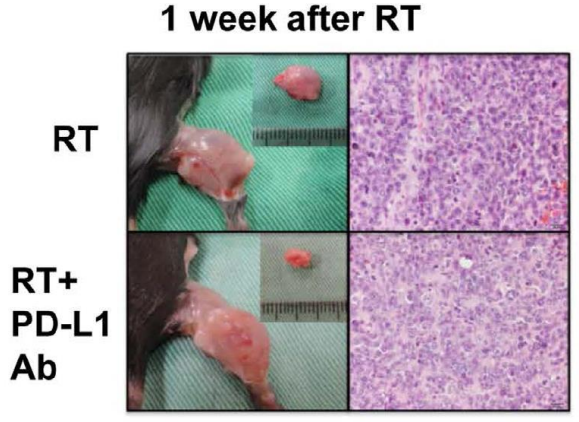
tomorrow



Buchwald & Efstathiou Bladder Cancer 2015

SCIENTIFIC REPORTS
OPEN
The role of PD-L1 in the radiation response and clinical outcome for bladder cancer

6:19740 | DOI: 10.1038/srep19740



conclusions

- Prostate cancer
  - Several active agents may be sequenced achieving unprecented cumulative survival gain.
  - Precision medicine is the driver of new agents development
- Renal cancer
  - Agents with new mechanism of action are able to overcome the risk of cross resistance compared the old agents
- Bladder cancer
  - Check point inhibitors, which weem to be able to achieve unprecented long term survival rates, should confirm these exciting results with long-term data

THANK YOU