

Perspectivas Futuras

Imunoterapia Câncer Urológico

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Cenário Atual



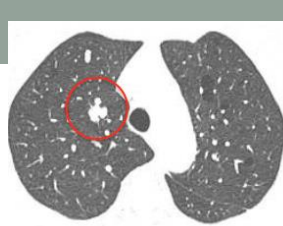
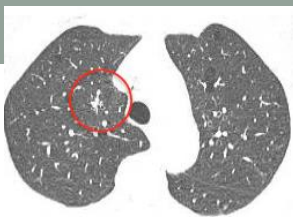
- ✓ Sipuleucel-T
- ✓ Nivo/Pembro (MSI-high)



- ✓ Nivolumabe
- ✓ Ipilimumabe+Nivolumabe
- ✓ Interferon; IL-2

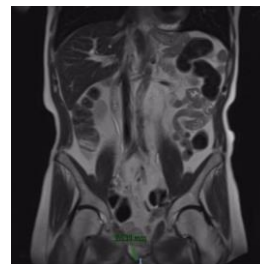
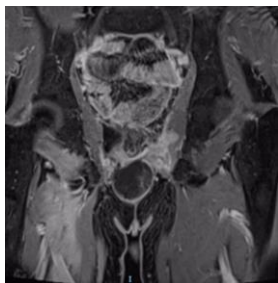


- ✓ Pembrolizumabe
- ✓ Nivolumabe
- ✓ Atezolizumabe
- ✓ Durvalumabe



M, 74a, CCR, metastático pulmão, risco intermediário, progressão após 6 m pazopanibe

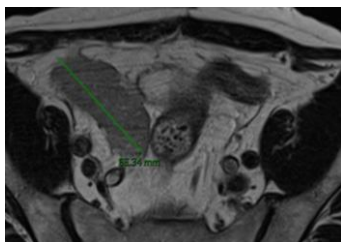
Resposta Mista



H, 70a, carcinoma urotelial diferenciação escamosa, progressão metástases durante QT neoadjuvante.

Sintomático

Resposta Completa



H, 83a, carcinoma urotelial pelve metástases peritoneais, 2 tumores prévios (próstata e estômago), outros casos familia. Não elegível cisplatina

Progressão maciça

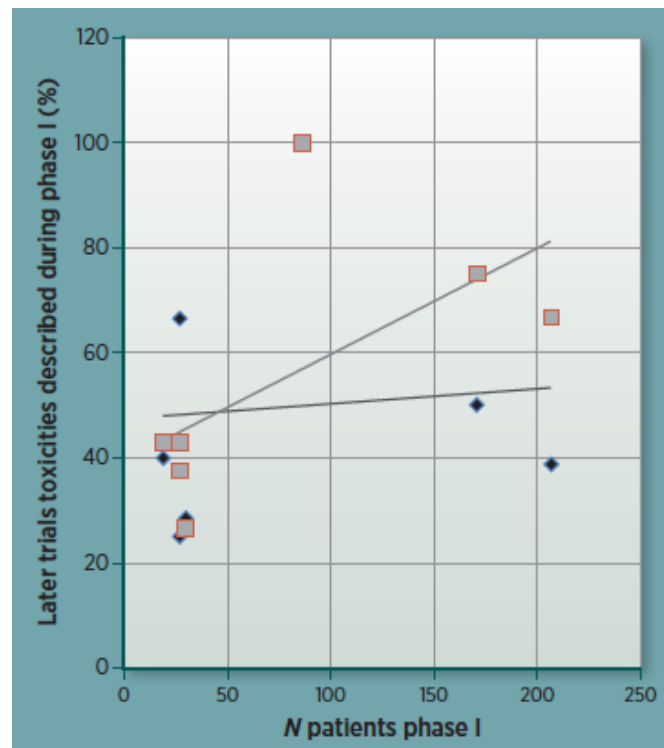
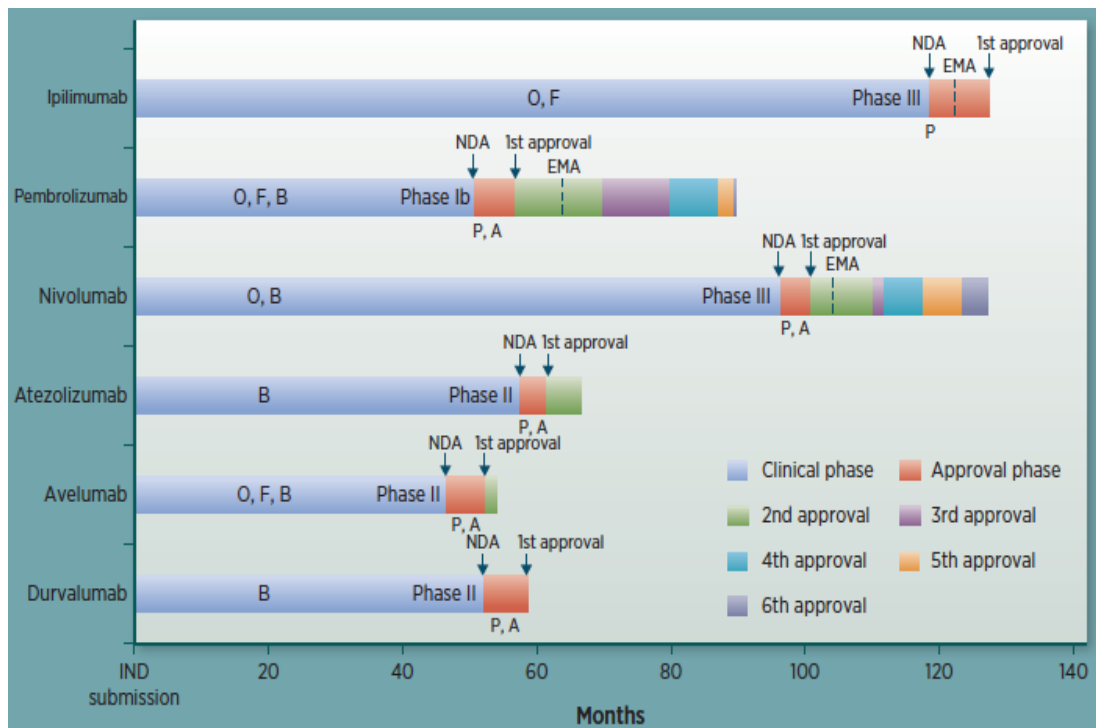
Desafios futuros

- Selecionar respondedores e não respondedores monoterapia
- Implementar combinações para melhora de eficácia
- Melhor definição tempo de tratamento, doses
- Novas modalidades imunoterapia

Analysis of Drug Development Paradigms for Immune Checkpoint inhibitors

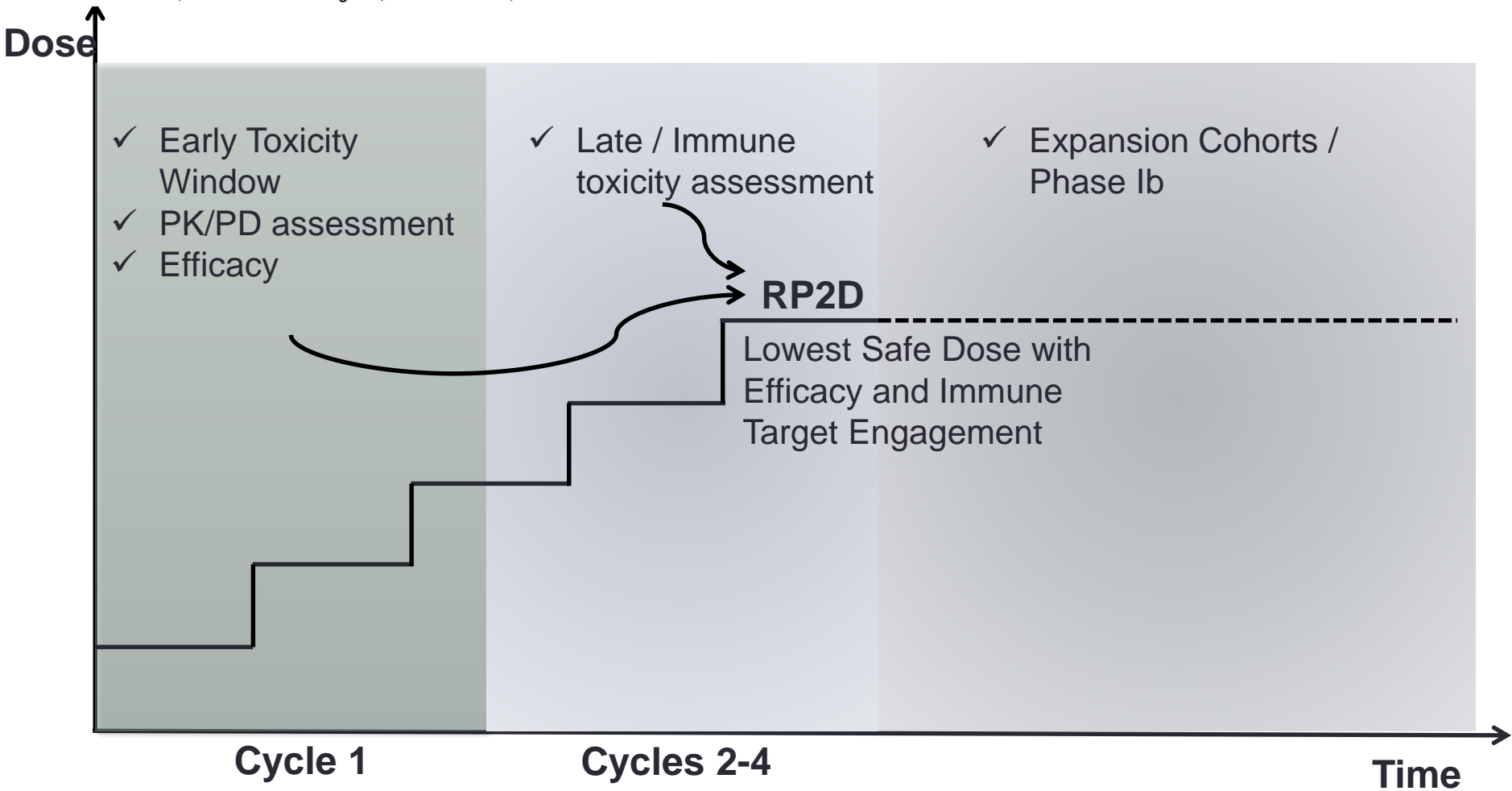
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Denis L. Jardim, Debora de Melo Gagliato, Francis J. Giles, and Razelle Kurzrock



Analysis of Drug Development Paradigms for Immune Checkpoint inhibitors

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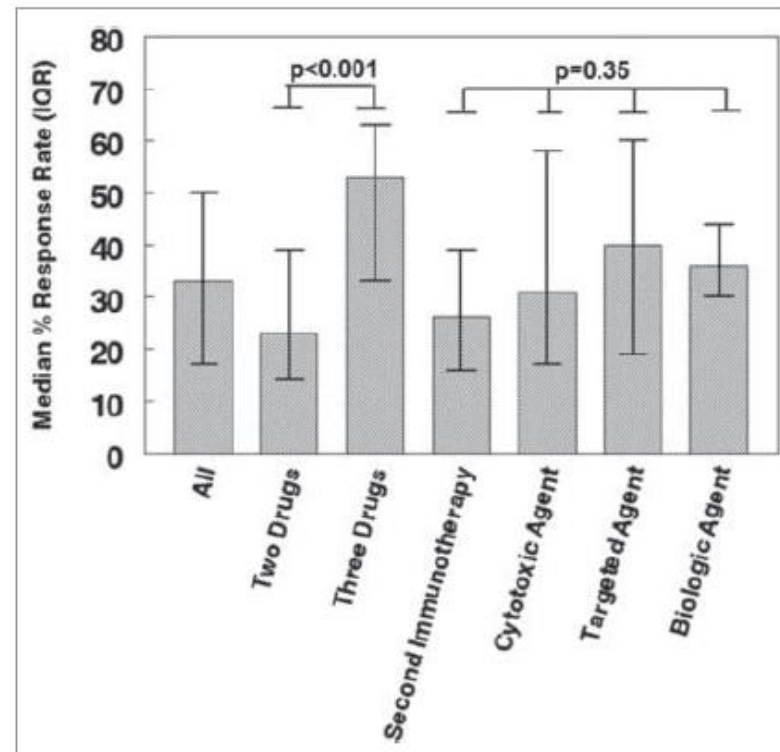
COMBINAÇÕES

Dosing immunotherapy combinations: Analysis of 3,526 patients for toxicity and response patterns

Doses

Two Drug Combinations	
Both Drugs 100% dose percentage of FDA/RP2D/MTD dose	
2 nd drug targeted agent (N = 22 studies)	59% of studies (13/22)
2 nd drug immunotherapy (N = 23 studies)	9% of studies (2/23)
2 nd drug cytotoxic chemotherapy (N = 10 studies)	50% of studies (5/10)
2 nd drug biologic agent (N=5 studies)	40% of studies (2/5)
Three Drug Combinations ^e	
All Three Drugs Each at 100% dose percentage of FDA/RP2D/MTD dose	
2 nd and 3 rd Drugs cytotoxic agents (N = 18 studies)	78% of studies (14/18)

Resposta



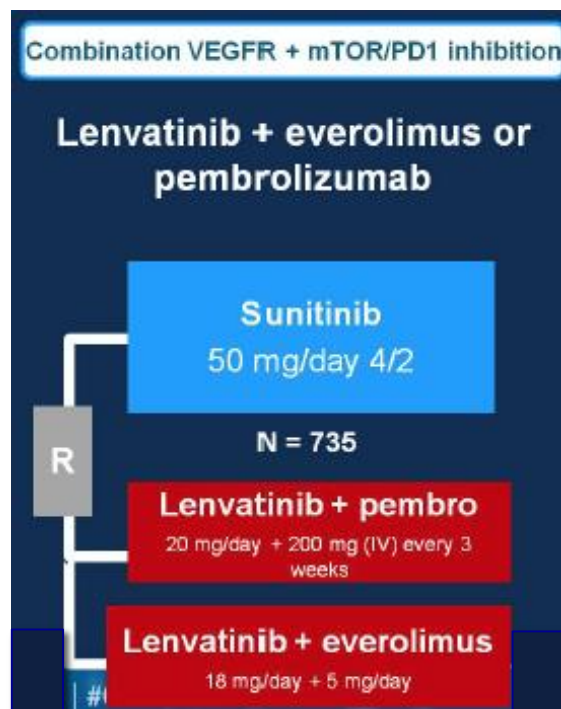
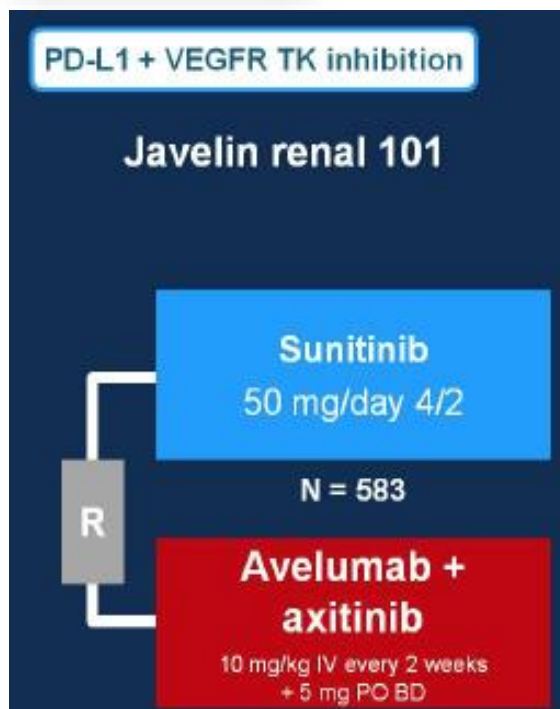


PD1/PD-L1 e VEGF

	Pembro + axitinib	Avelumab + axitinib	Pembro + lenvatinib	Atezo + bevacizumab	Nivo + Tivozanib
n	52	45	30	101	14
CR	5.8%	5.5%	0	7%	0
PR	65.4%	52.7%	63%	25%	64.3%
ORR	71.2% (73.1%)*	58.2%	63%	32%	64.3%

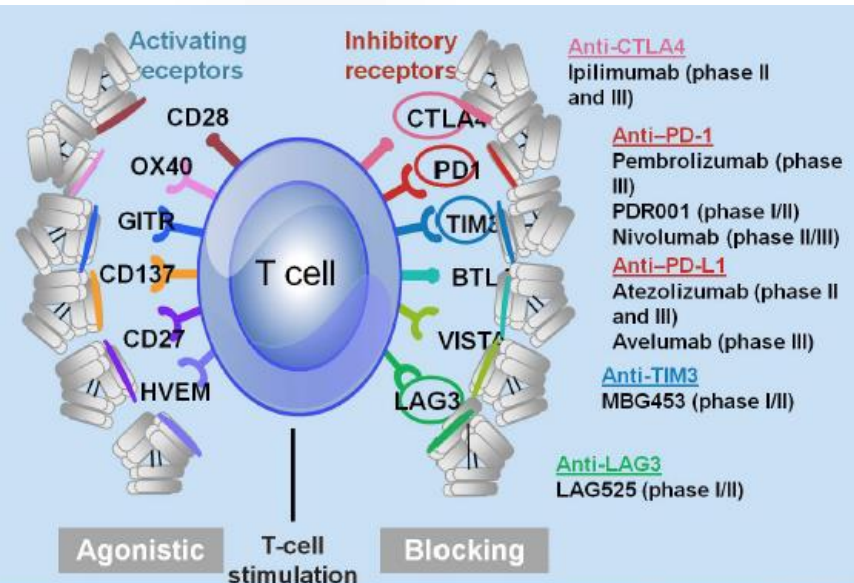


PD1/PD-L1 e VEGF Fase III





Combinações Imuno



- ✓ Anti PD-1 + Anti LAG 3
 - ✓ Pré-clínico
- ✓ Anti PD-1 + Peg IL10
- ✓ Anti PD-1 + anti IDO1 (Epacadostat)



PD1/PD-L1+quimioterapia+/- immuno

NCT02807636 (IMvigor130):¹ N=1,200

- First-line cisplatin-ineligible, locally advanced/metastatic
- ECOG PS ≤ 2

Co-primary endpoints: PFS, OS and safety

NCT02516241 (DANUBE):² N=1,005

- First-line unresectable stage IV
- Eligible/ineligible for cisplatin-based chemotherapy

Co-primary endpoints: PFS and OS

NCT02853305 (KEYNOTE-361):³ N=990

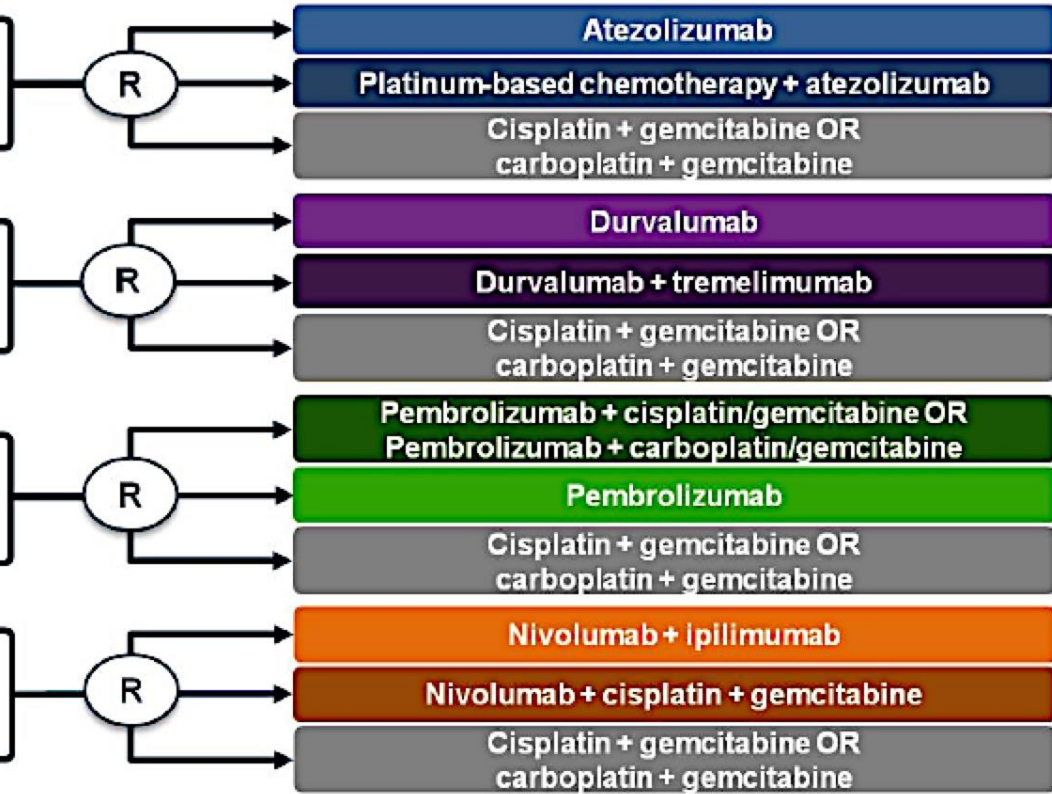
- First-line unresectable or metastatic
- ECOG PS ≤ 2

Co-primary endpoints: PFS and OS

NCT03036098 (CheckMate-901):⁴ N=897

- First-line unresectable or metastatic
- ECOG PS ≤ 1

Co-primary endpoints: PFS and OS

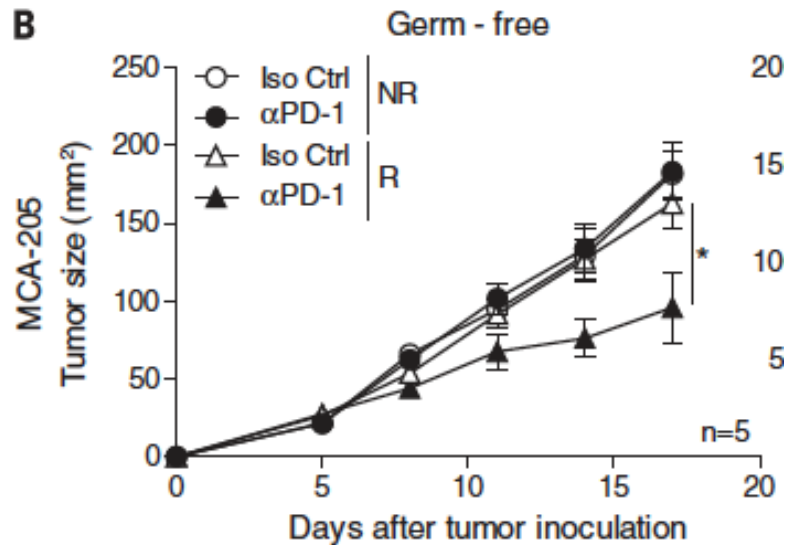
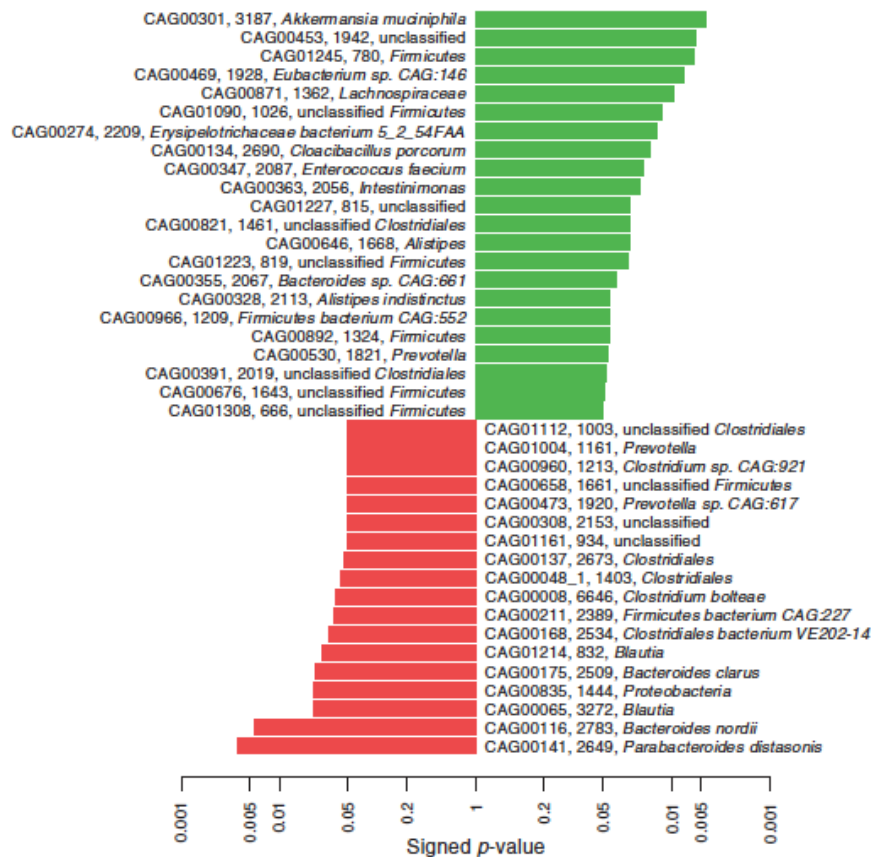


NOVOS FATORES

Microbiota

B

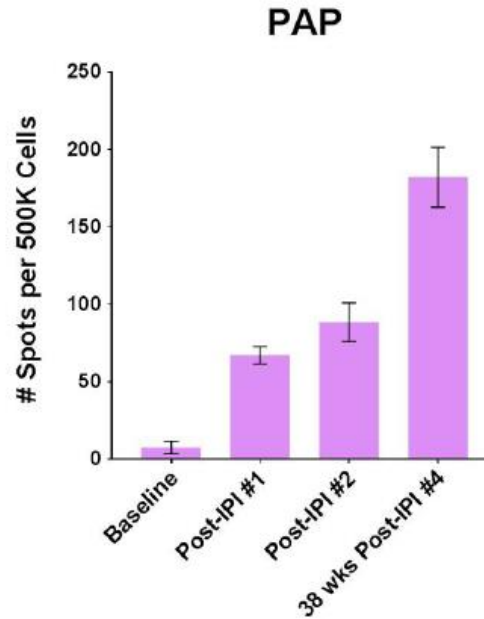
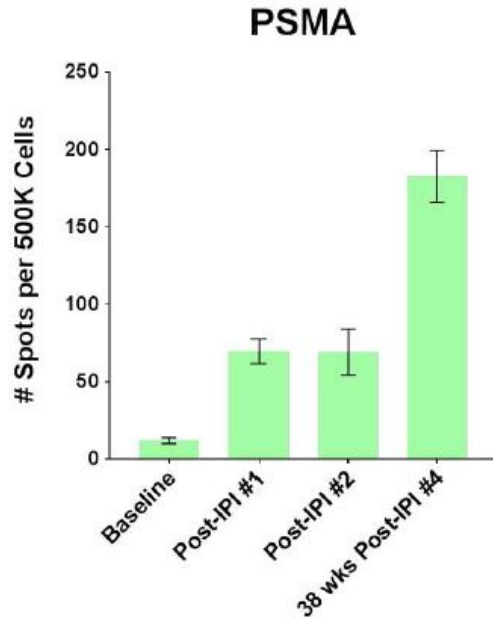
- Enriched in R: Objective response (PR and SD)
- Enriched in NR: Objective response (PD or death)





Novos antígenos e estratégias

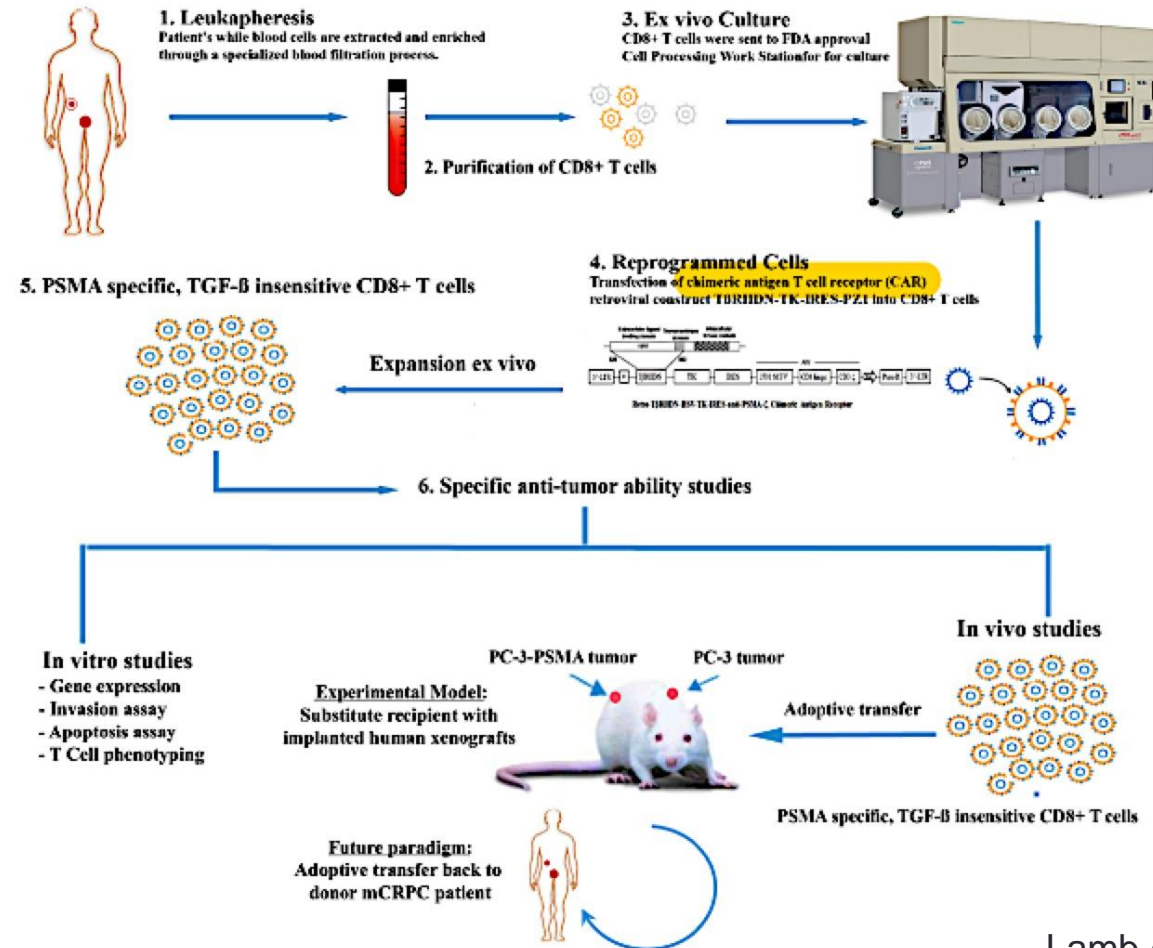
Respostas de Células T a antígenos prostáticos



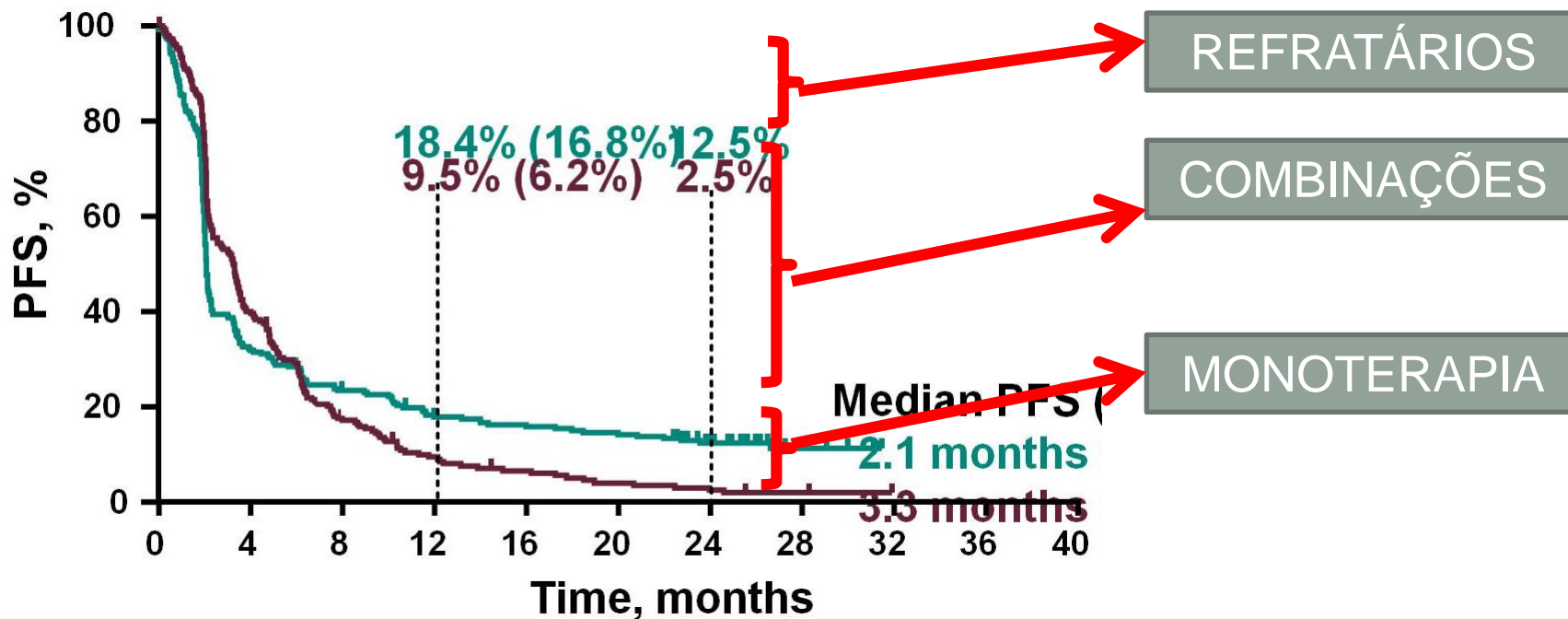
- ✓ Influencia de outros check-points (VISTA)
- ✓ Estratégias para tornar o tumor “inflamado”

First Report of Prostate-specific Membrane Antigen-targeted Immunotherapy in Prostate Cancer: The Future is Bright

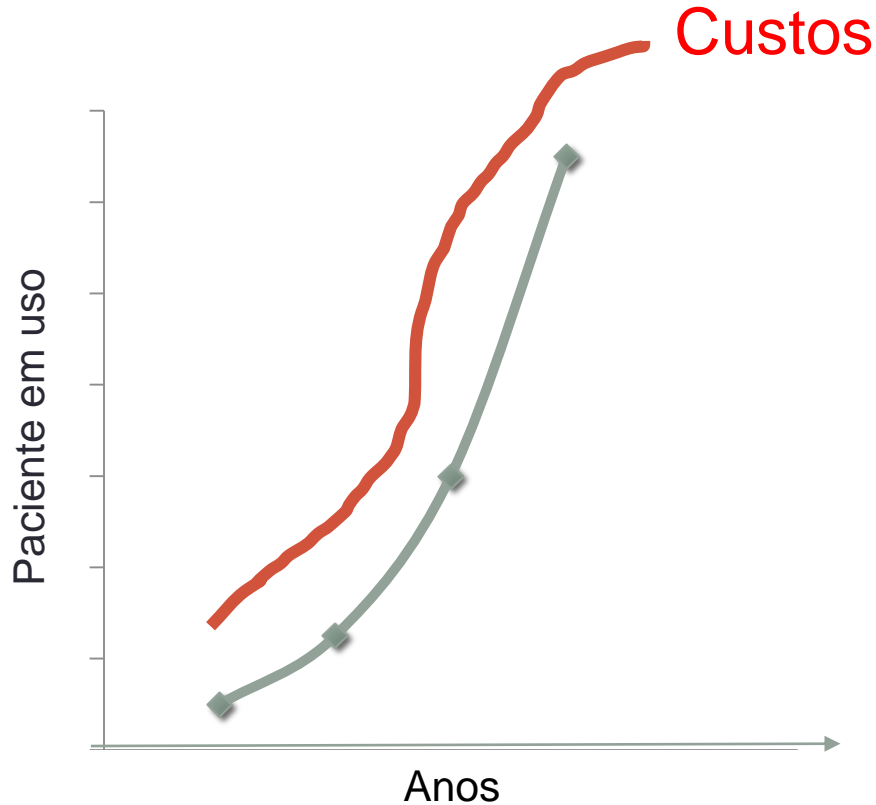
mCRPC patient



Paradigma Futuro



Paradigma Futuro



- ✓ Tratamentos imunoterápicos serão administrados por oncologistas (inclusive da comunidade)
- ✓ Maior número de doenças localizadas serão curadas mesmo sem cirurgia
- ✓ Pequenos planos de saúde e clínicas possivelmente não se sustentarão
- ✓ Acordos comerciais indústria serão necessários

OBRIGADO

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