



Healthy DrivenTM

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HEALTH



Elmhurst Primary Care Conference 2021: Oncology

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Hematology/Medical Oncology
Edward-Elmhurst Health

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Disclosures

- none

FDA Off label use

- I will be discussing the off label use of agents

A Brief History of Systemic Cancer Treatments (Chemotherapy)

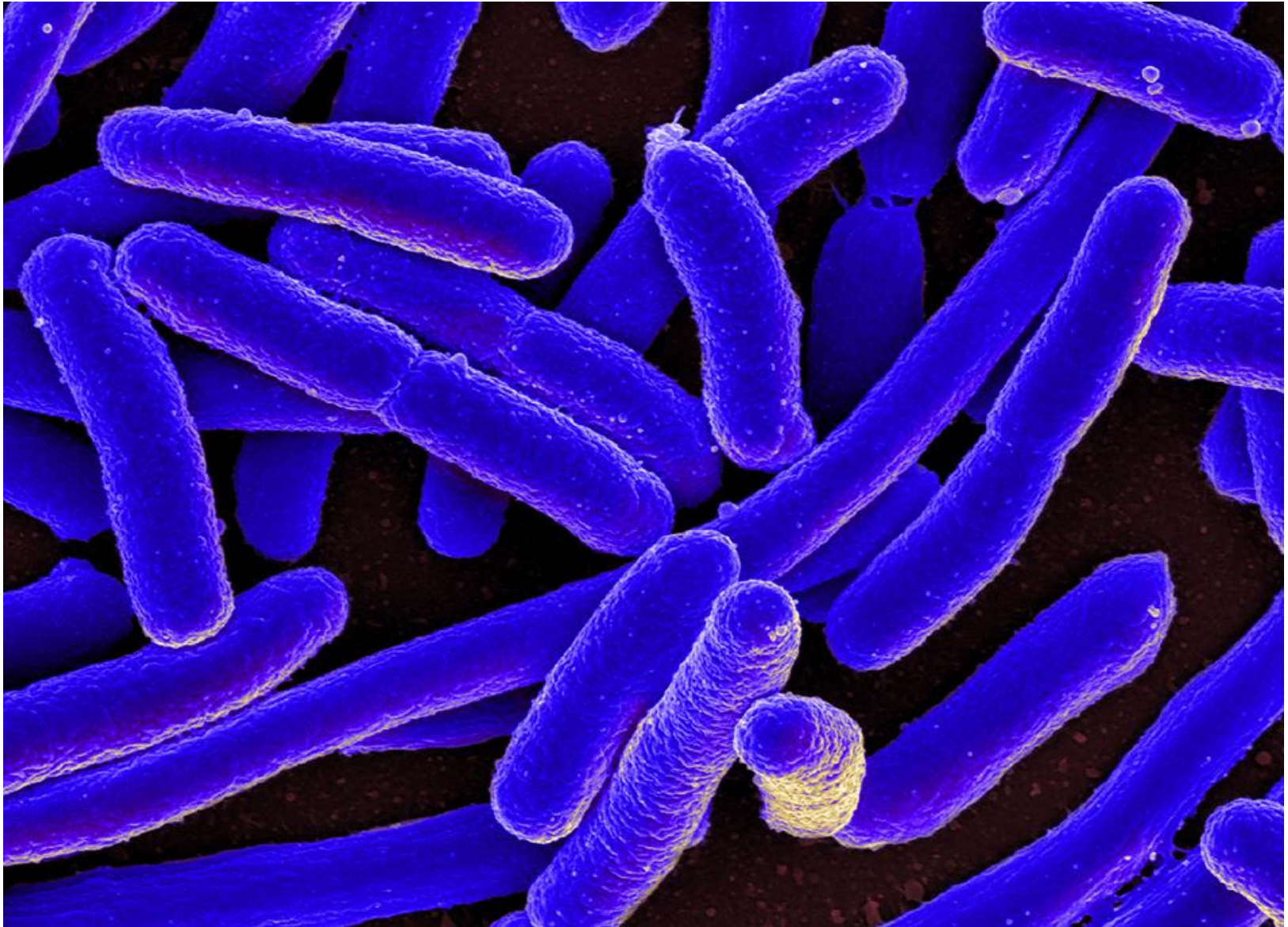
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Chemotherapy

- 1960: NCI commissioned the [United States Department of Agriculture](#) (USDA) botanists to collect samples from about 1,000 plant species per year.
- 1962: botanist Arthur S. Barclay, collected bark from a single Pacific yew tree in a forest north of the town of [Packwood, Washington](#) as part of a four-month trip to collect material from over 200 different species.
- The material was then processed and one of the tree's samples was found to be [cytotoxic](#) in a cellular assay on 22 May 1964

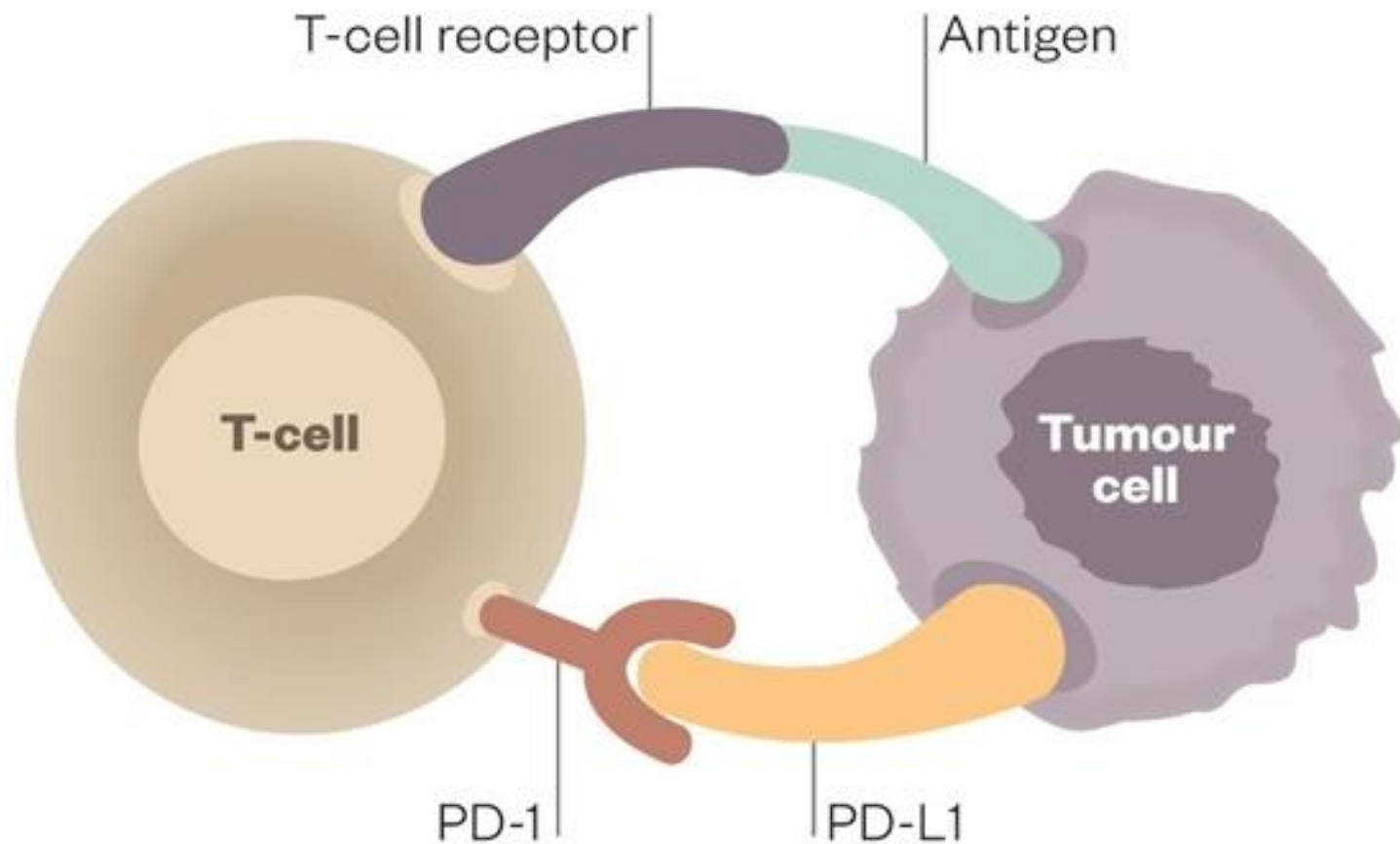
Chemotherapy

- Toxicities:
 - Bone marrow suppression
 - Mucositis
 - Nausea and vomiting
 - Neuropathy
 - Alopecia

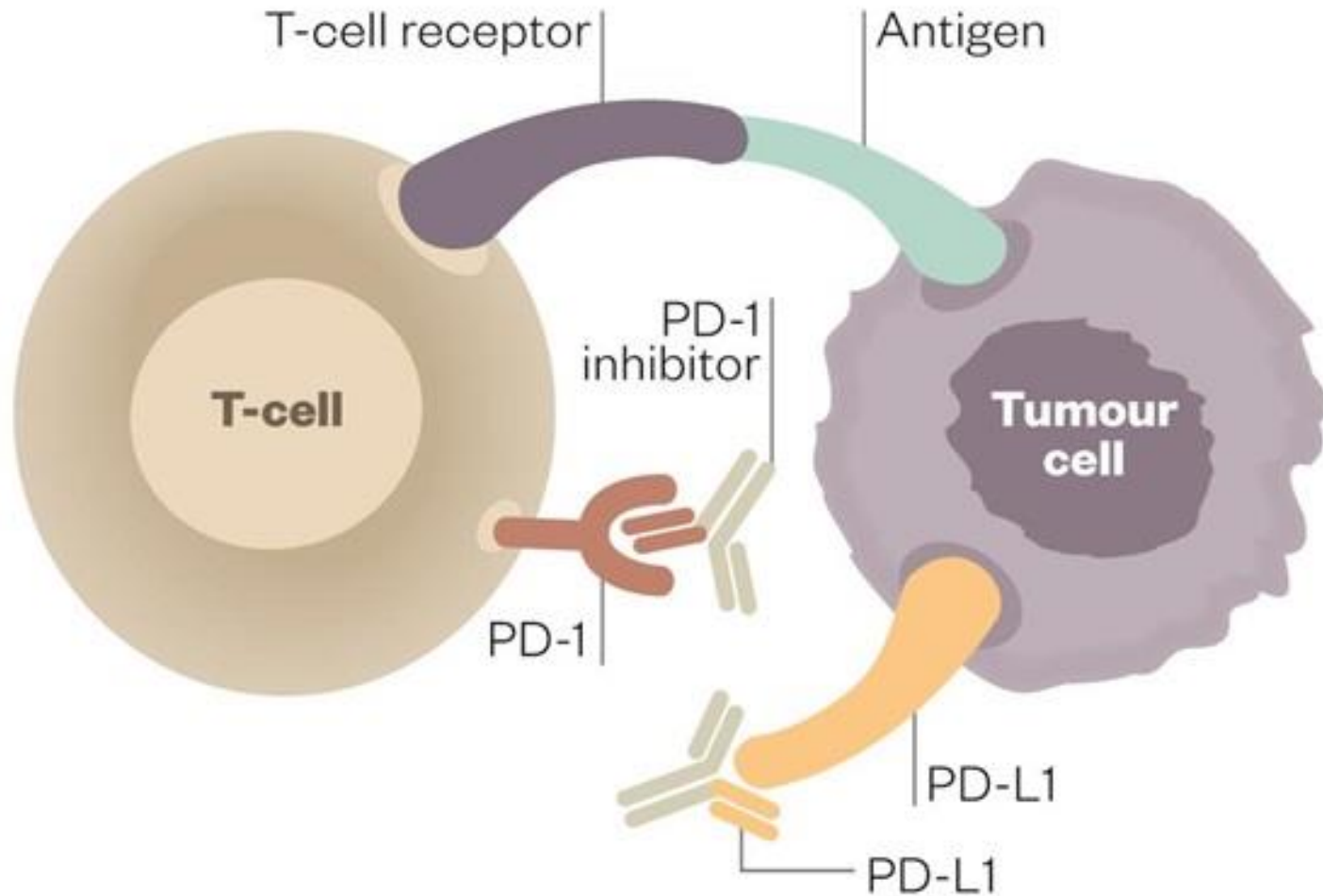
Modern Cancer Treatment

- **T-cell Immunotherapy**
 - **Immune checkpoint Inhibitors (PD1/PDL1)**
- **Genome guided therapy**
- **Hormone Therapy**

What is PD-1/PD-L1?



What is PD-1/PD-L1?



Immunotherapy: 1st Line FDA Approvals

- Melanoma
- Head and Neck
- Lung
- Renal
- Bladder/Urothelial
- Breast (triple negative)

Pending FDA review:

- **Gastric**

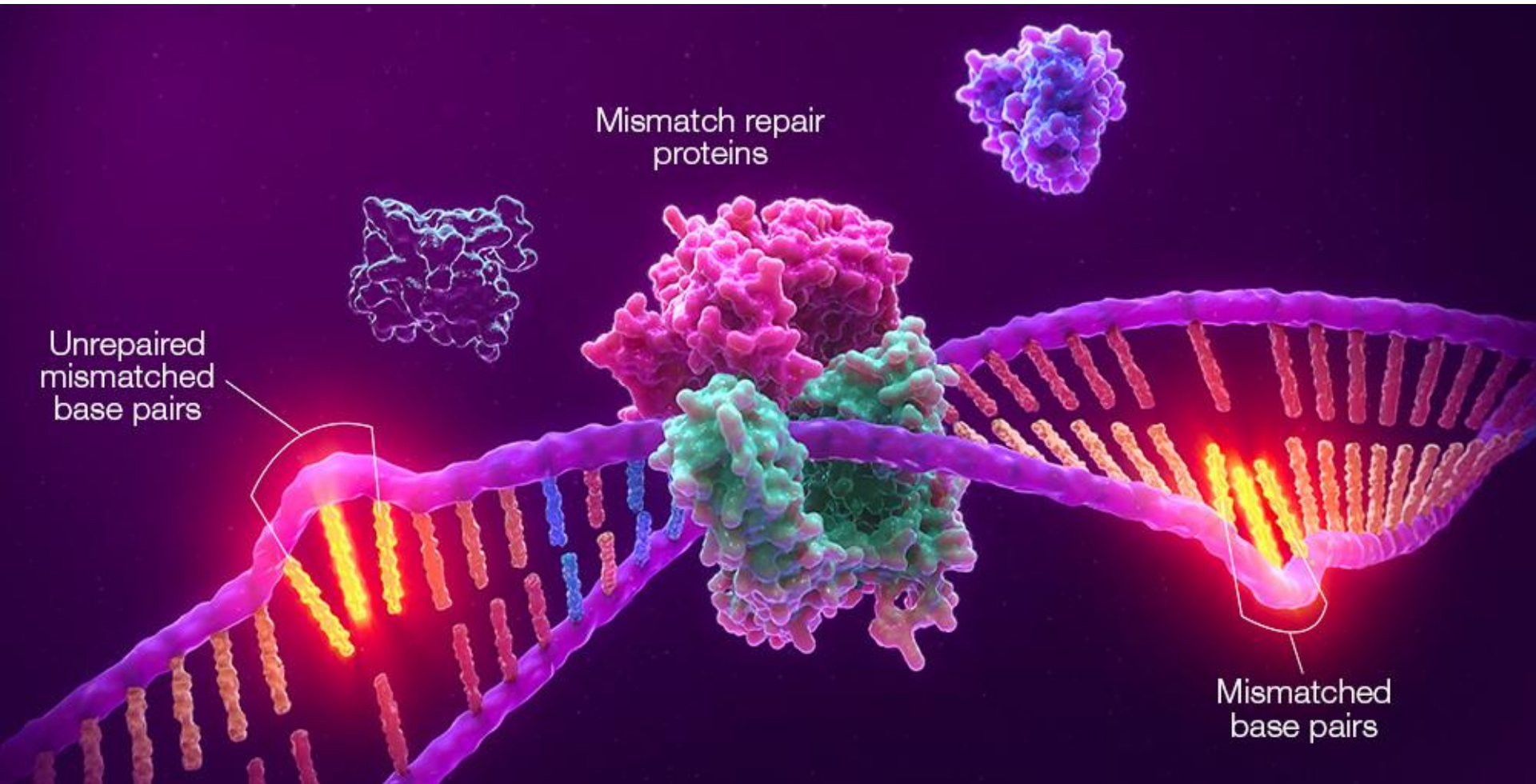
- ESMO: September 2020

- Chemotherapy vs chemotherapy with nivolumab
 - Adding nivolumab improved progression free survival and overall survival
 - OS: 14.4 months when PDL1 >5%

- Moehler M, Shitara K, Garrido M, et al: Nivolumab plus chemotherapy vs chemo as first-line treatment for advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma: First results of the CheckMate 649 study. ESMO Virtual Congress 2020. Abstract LBA6_PR. Presented September 21, 2020.

Immunotherapy

- Microsatellite instability/Deficiency in Mismatch Repair

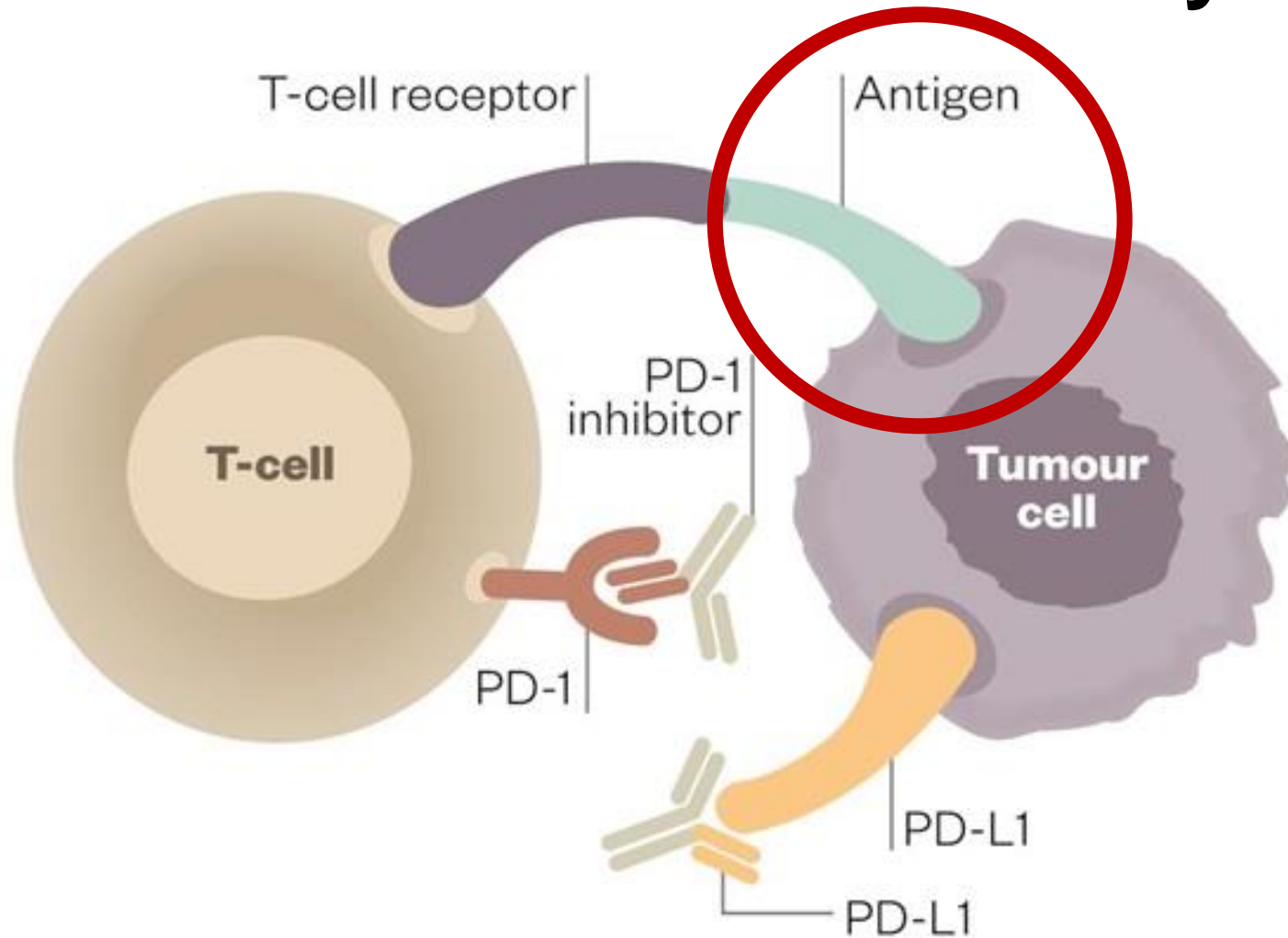


Unrepaired mismatched base pairs

Mismatch repair proteins

Mismatched base pairs

What is Microsatellite Instability?



Immunotherapy

- Microsatellite instability/Deficiency in Mismatch Repair
 - 2017: FDA Approved Pembrolizumab tissue/site agnostic if MSI/dMMR
 - progressed following standard of care chemotherapy

Immunotherapy

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ESTABLISHED IN 1812

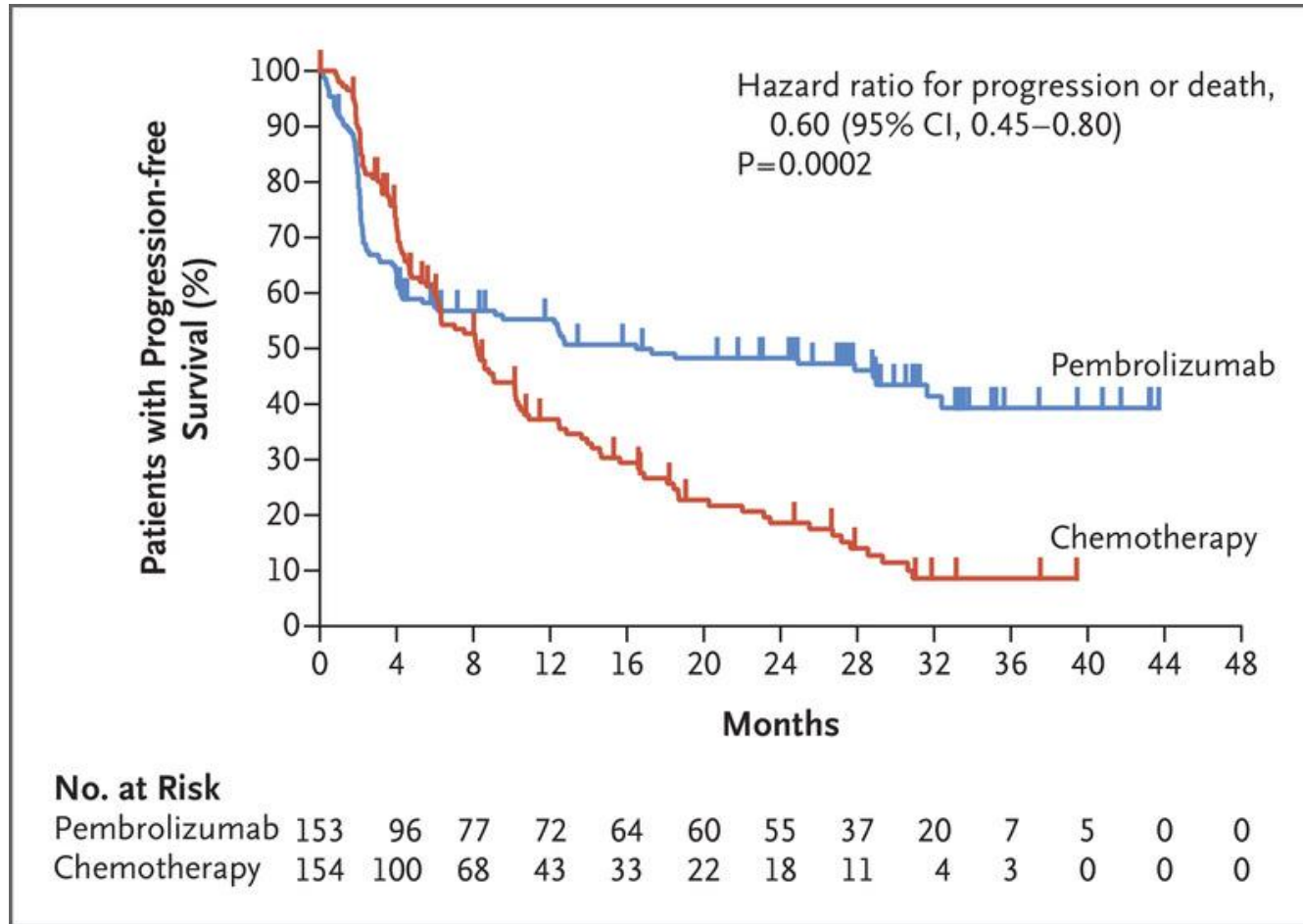
DECEMBER 3, 2020

VOL. 383 NO. 23

Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer

T. André, K.-K. Shiu, T.W. Kim, B.V. Jensen, L.H. Jensen, C. Punt, D. Smith, R. Garcia-Carbonero, M. Benavides, P. Gibbs, C. de la Fouchardiere, F. Rivera, E. Elez, J. Bendell, D.T. Le, T. Yoshino, E. Van Cutsem, P. Yang, M.Z.H. Farooqui, P. Marinello, and L.A. Diaz, Jr., for the KEYNOTE-177 Investigators*

Microsatellite Instability



Immunotherapy: 1st Line FDA Approvals

- Melanoma
- Head and Neck
- Lung
- Renal
- Bladder/Urothelial
- Breast (triple negative)
- ***Colon (Microsatellite-instability high)***
- ***Pending: Gastric***

Genomics

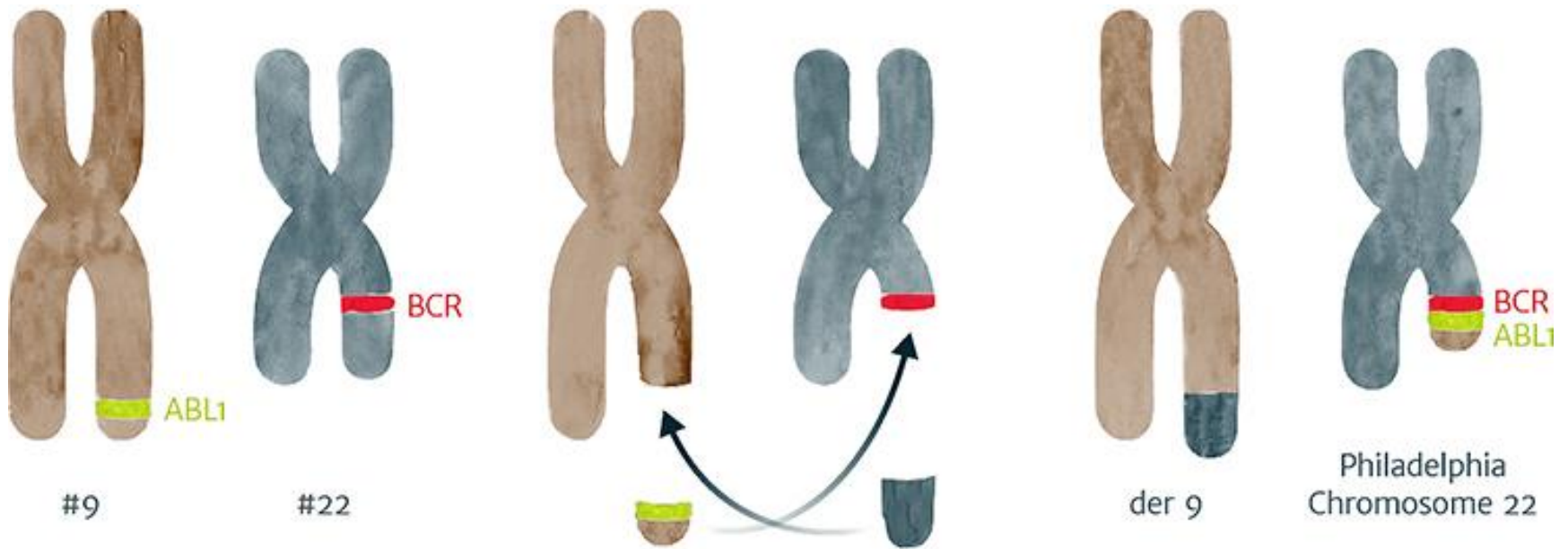


Genomics



"TEMPUS





- 2001: FDA approves Imatinib (Gleevac) for CML

Genomics

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ORIGINAL ARTICLE

Efficacy of Larotrectinib in *TRK* Fusion-Positive Cancers in Adults and Children

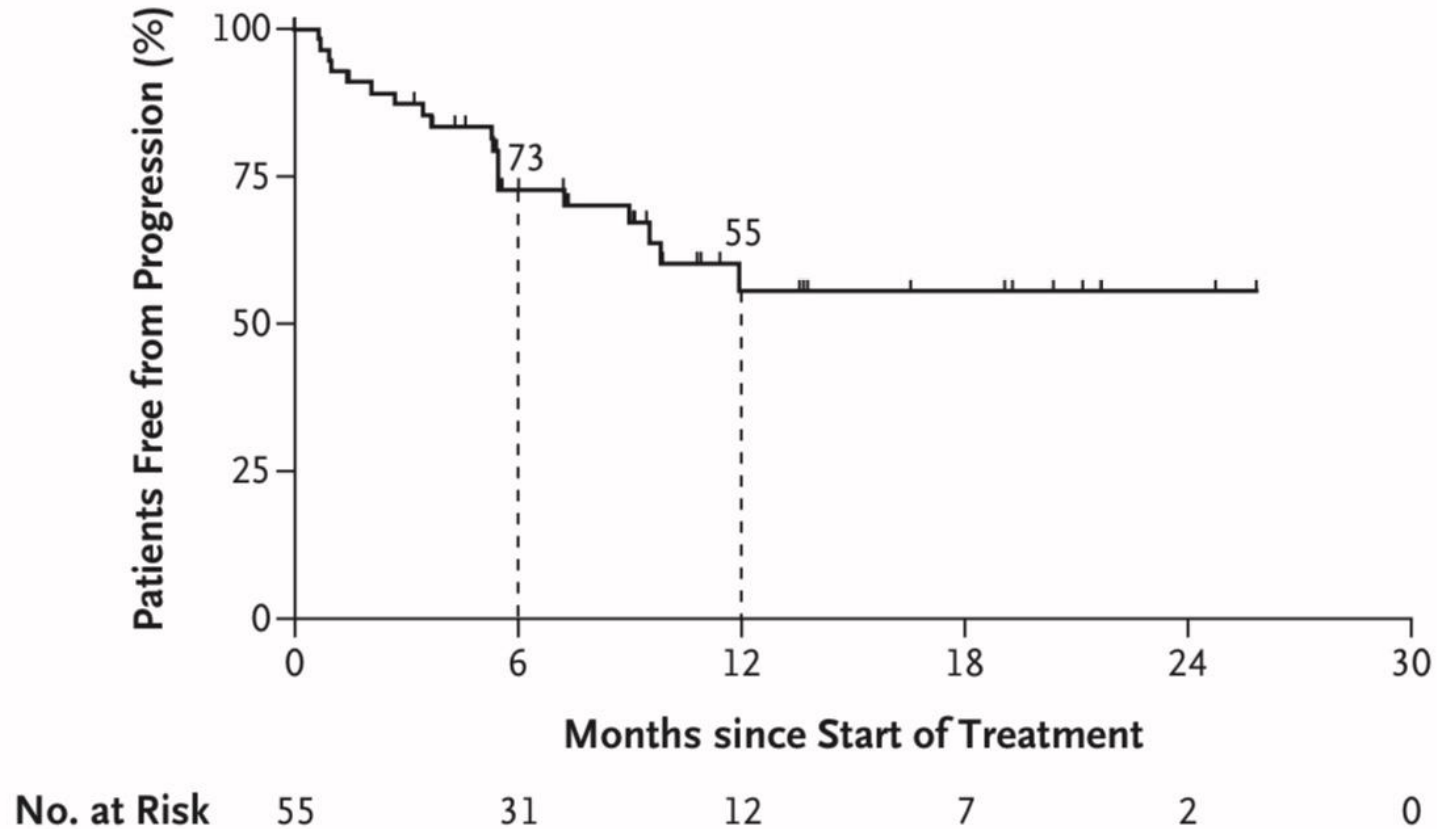
A. Drilon, T.W. Laetsch, S. Kummar, S.G. DuBois, U.N. Lassen, G.D. Demetri, M. Nathenson, R.C. Doebele, A.F. Farago, A.S. Pappo, B. Turpin, A. Dowlati, M.S. Brose, L. Mascarenhas, N. Federman, J. Berlin, W.S. El-Deiry, C. Baik, J. Deeken, V. Boni, R. Nagasubramanian, M. Taylor, E.R. Rudzinski, F. Meric-Bernstam, D.P.S. Sohal, P.C. Ma, L.E. Raez, J.F. Hechtman, R. Benayed, M. Ladanyi, B.B. Tuch, K. Ebata, S. Cruickshank, N.C. Ku, M.C. Cox, D.S. Hawkins, D.S. Hong, and D.M. Hyman

Genomics

Tumor type — no. (%)	
Salivary-gland tumor	12 (22)
Other soft-tissue sarcoma‡	11 (20)
Infantile fibrosarcoma	7 (13)
Thyroid tumor	5 (9)
Colon tumor	4 (7)
Lung tumor	4 (7)
Melanoma	4 (7)
GIST	3 (5)
Cholangiocarcinoma	2 (4)
Appendix tumor	1 (2)
Breast tumor	1 (2)
Pancreatic tumor	1 (2)

Genomics

B Progression-free Survival among All Patients



Genomics

- BRCA
 - Breast Cancer gene

Genomics

- December 2020
- BRCA1/2, ATM

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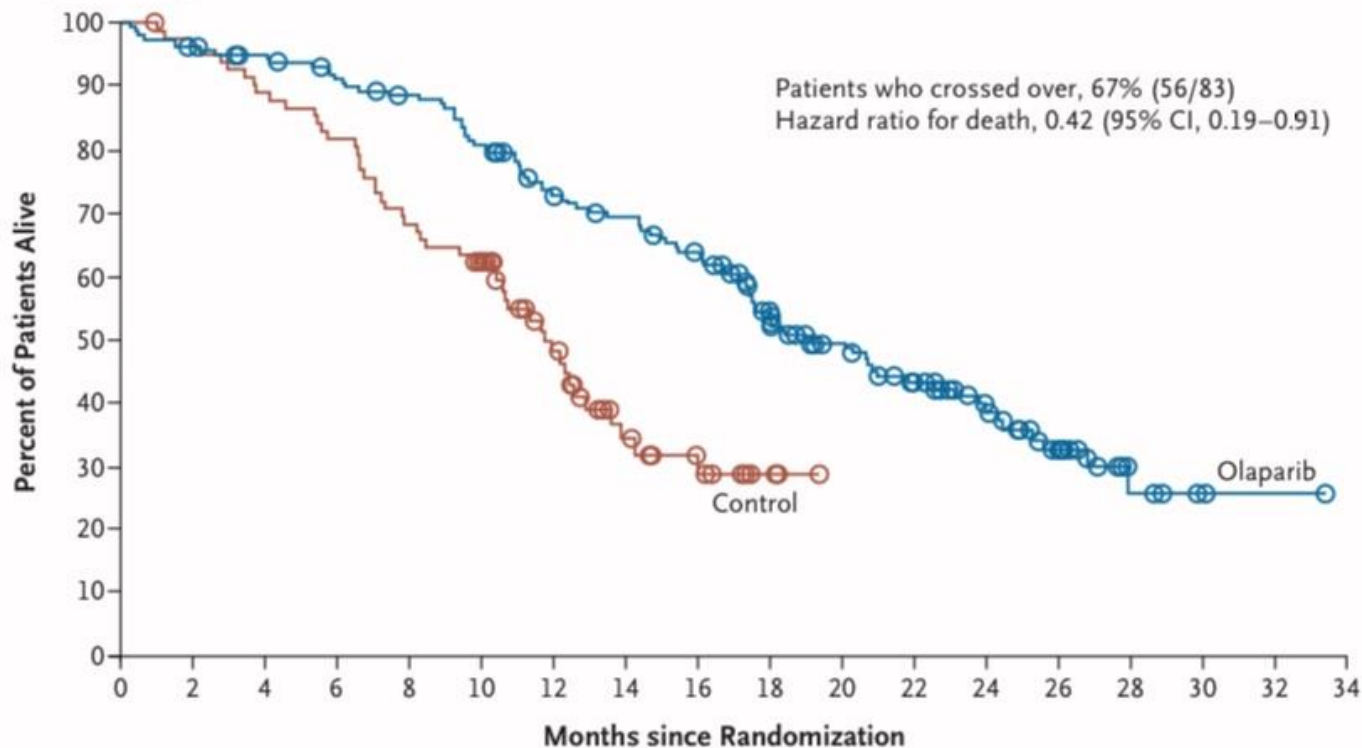
ORIGINAL ARTICLE

Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

M. Hussain, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor, N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, G. Roubaud, M. Özgüroğlu, J. Kang, J. Burgents, C. Gresty, C. Corcoran, C.A. Adelman, and J. de Bono, for the PROfound Trial Investigators*

Genomics

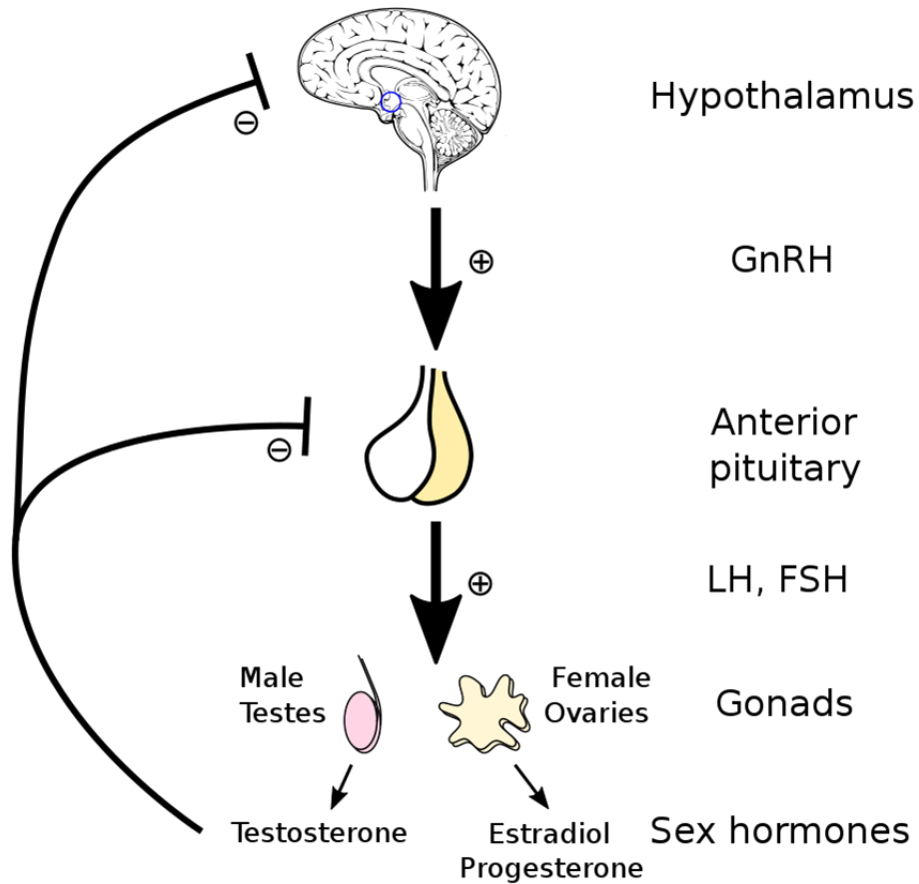
B Crossover-Adjusted Analysis of Overall Survival in Cohort A



No. at risk
Olaparib
Control

162	155	150	142	136	124	107	101	91	71	56	44	30	18	6	2	1	0
83	79	73	67	56	47	29	15	9	3	0	0	0	0	0	0	0	0

Hormonal Therapies



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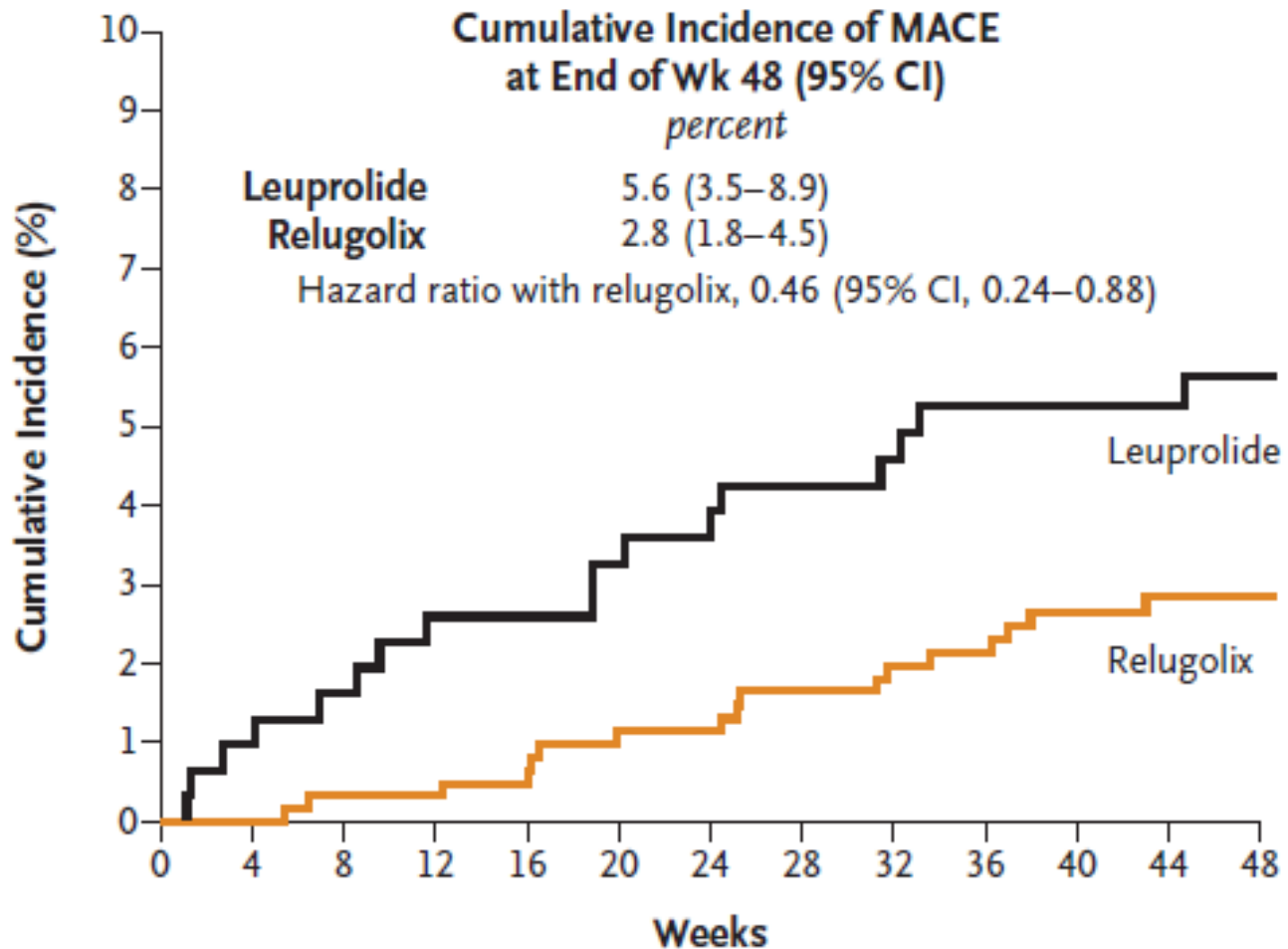
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Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer

Neal D. Shore, M.D., Fred Saad, M.D., Michael S. Cookson, M.D., M.M.H.C., Daniel J. George, M.D.,
Daniel R. Saltzstein, M.D., Ronald Tutrone, M.D., Hideyuki Akaza, M.D., Alberto Bossi, M.D.,
David F. van Veenhuizen, M.B., Ch.B., M.Pharm.Med., Bryan Selby, M.S., Xiaolin Fan, Ph.D., Vicky Kang, M.D.,
Jackie Walling, M.B., Ch.B., Ph.D., and Bertrand Tombal, M.D., Ph.D., for the HERO Study Investigators*



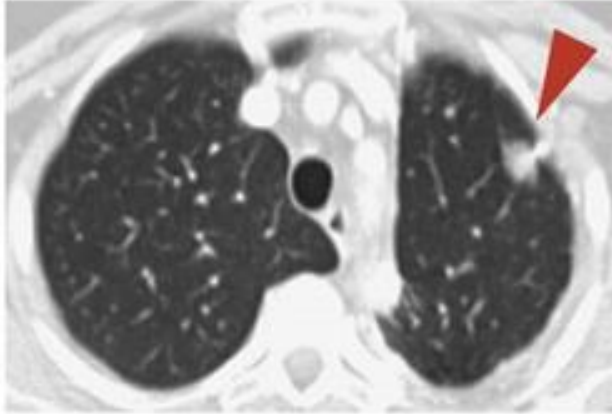
No. at Risk

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

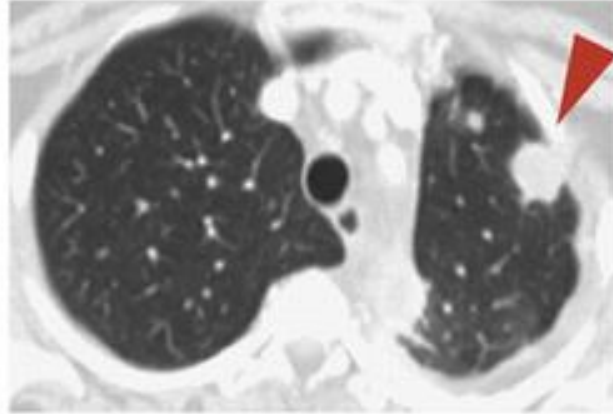
Immune Checkpoint Inhibitors

- Timing of Response and Toxicity
- Toxicity profile

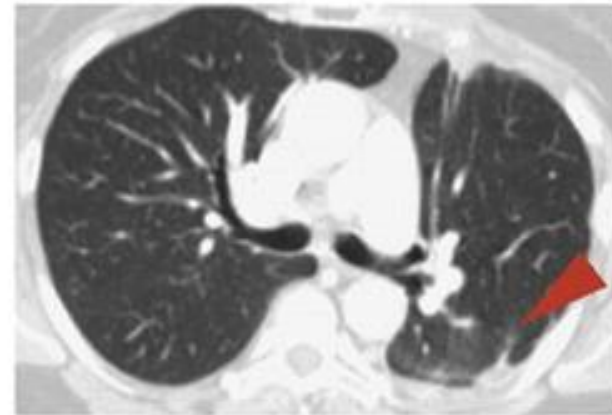
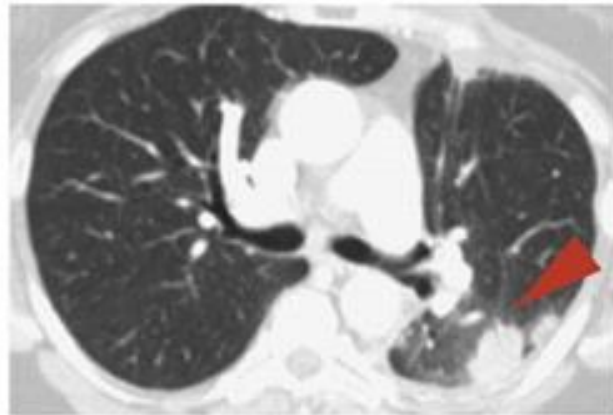
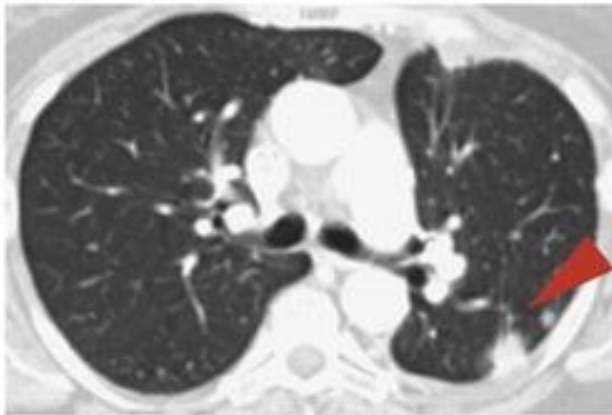
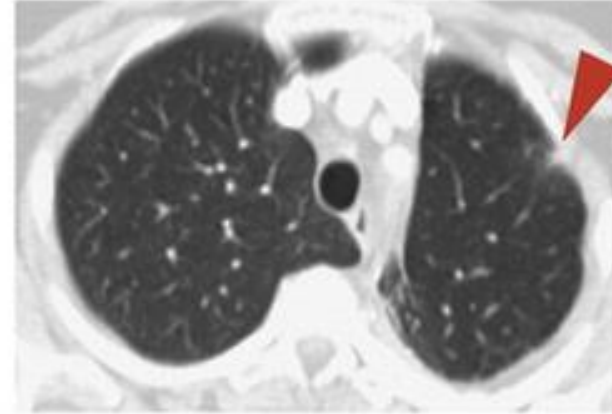
Before Treatment

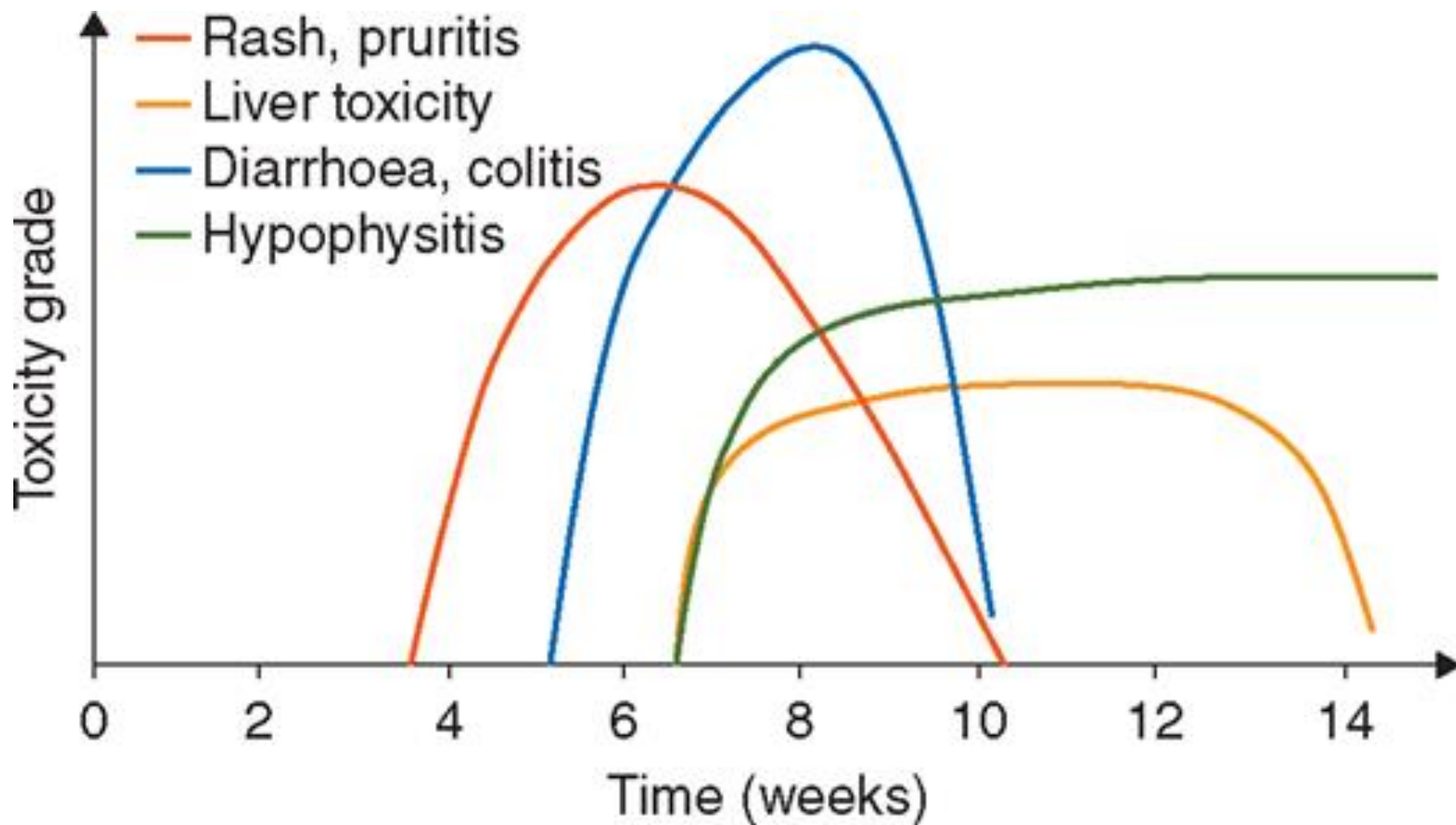


2 Months



4 Months





Immunotherapy Toxicity

- Autoimmune Manifestations
 - Pneumonitis
 - Dermatitis/Bullous Dermatosi
 - Colitis
 - Hepatitis
 - Pancreatitis → diabetes
 - Endocrinopathies
 - Myocarditis

Adverse Events

- Endocrinopathies
 - Adrenal insufficiency/crisis
 - 0.7% in trials
 - Hypotension, hyponatremia, hyperkalemia
 - Hypo or Hyperthyroidism
 - Hypophysitis—pituitary inflammation
 - Distinguish from primary adrenal or thyroid abnormalities
 - FSH, LH, ACTH, TSH, Prolactin, Growth Hormone
 - Can give 1mg/kg prednisone daily

Immunotherapy Toxicity

- Autoimmune Manifestations
 - Treatment:
 - Moderate: prednisone 0.5-1mg/kg day
 - Severe/Life Threatening: prednisone 2mg/kg/day equivalent
 - If no improvement in 48-72 hours → Infliximab 5mg/kg
 - Further immunosuppression (mycophenolate mofetil, etc)

Immunotherapy– What to know

- Delayed onset
 - Disease response
 - Toxicity
- Autoimmune manifestations and Endocrinopathies

Thank you

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