(clinical) Updates on immunotherapy for Lynch syndrome cancer patients

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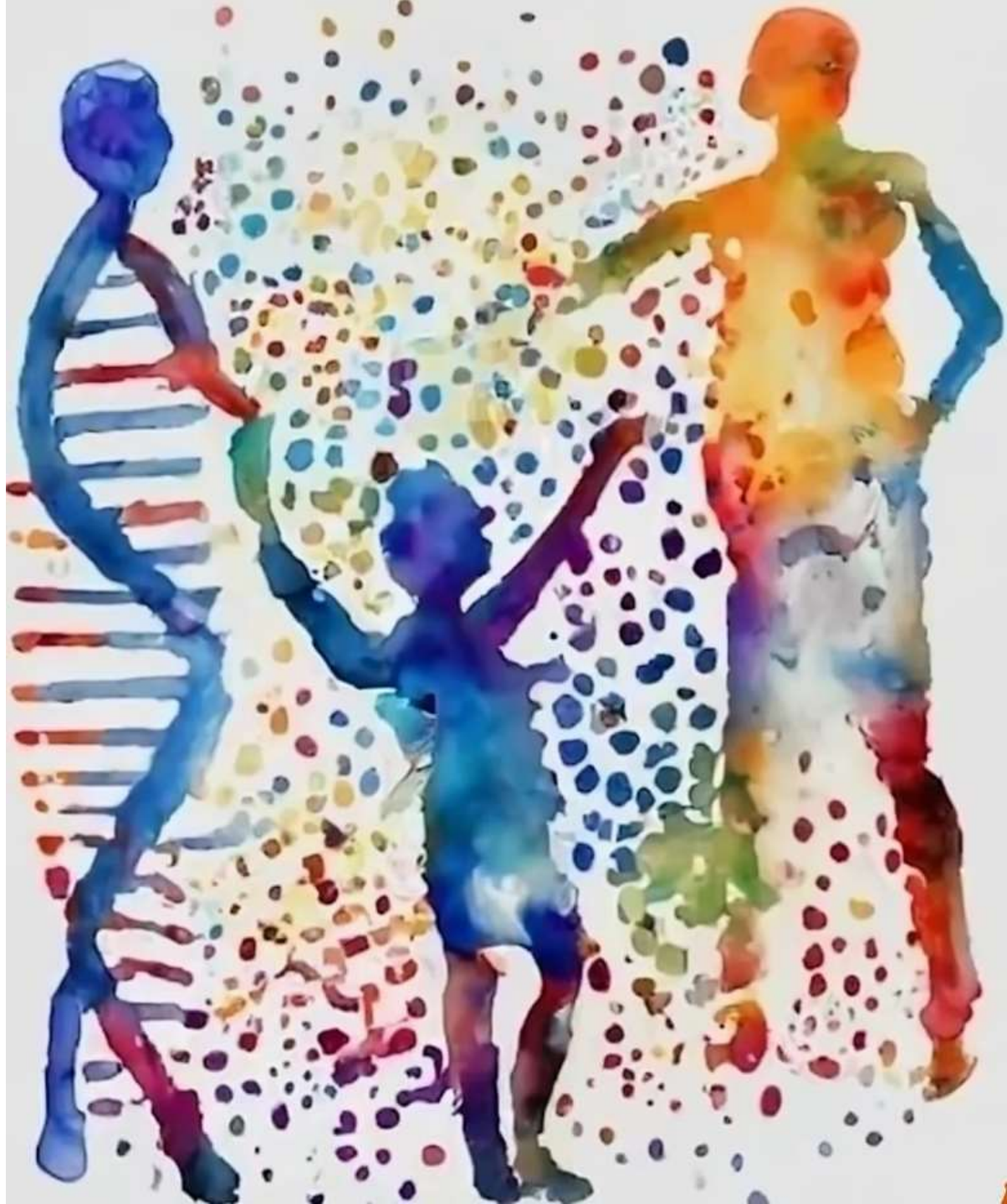


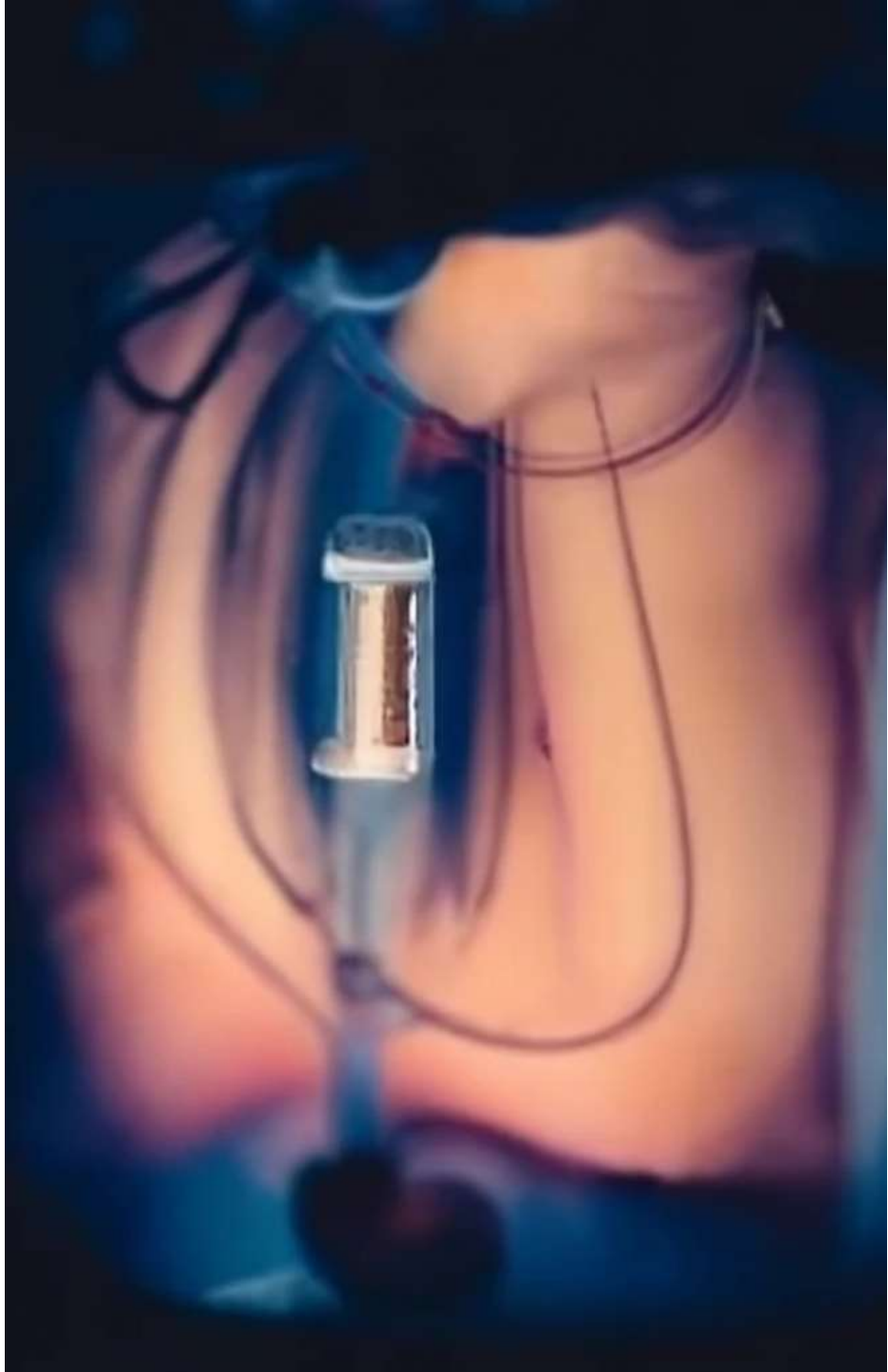
Outline

- Immunotherapy to Lynch – what are the clinical options?
- Randomized trials
- Standard immunotherapy to dMMR in Denmark
- Neoadjuvant (other session)
- Genomic profiling
- ProTarget – national protocol

Randomized trials

- First-line pembrolizumab
  - Improved progression-free survival
  - Improved quality of life
  - Unfortunately, Lynch not specified

- Nivolumab and ipilimumab, first and later
  - Inclusion finalized
  - Lynch reported
  - Database lock Nov 15, 2023 for first interim analysis

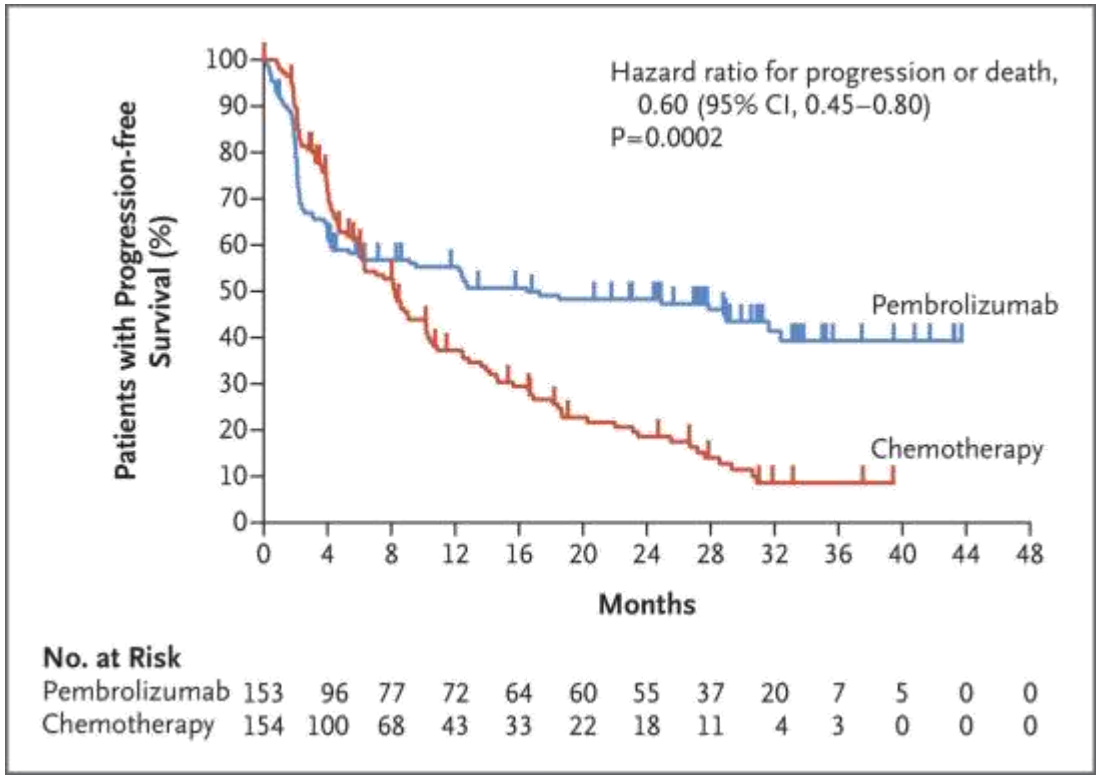


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 3, 2020 VOL. 383 NO. 23

Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer

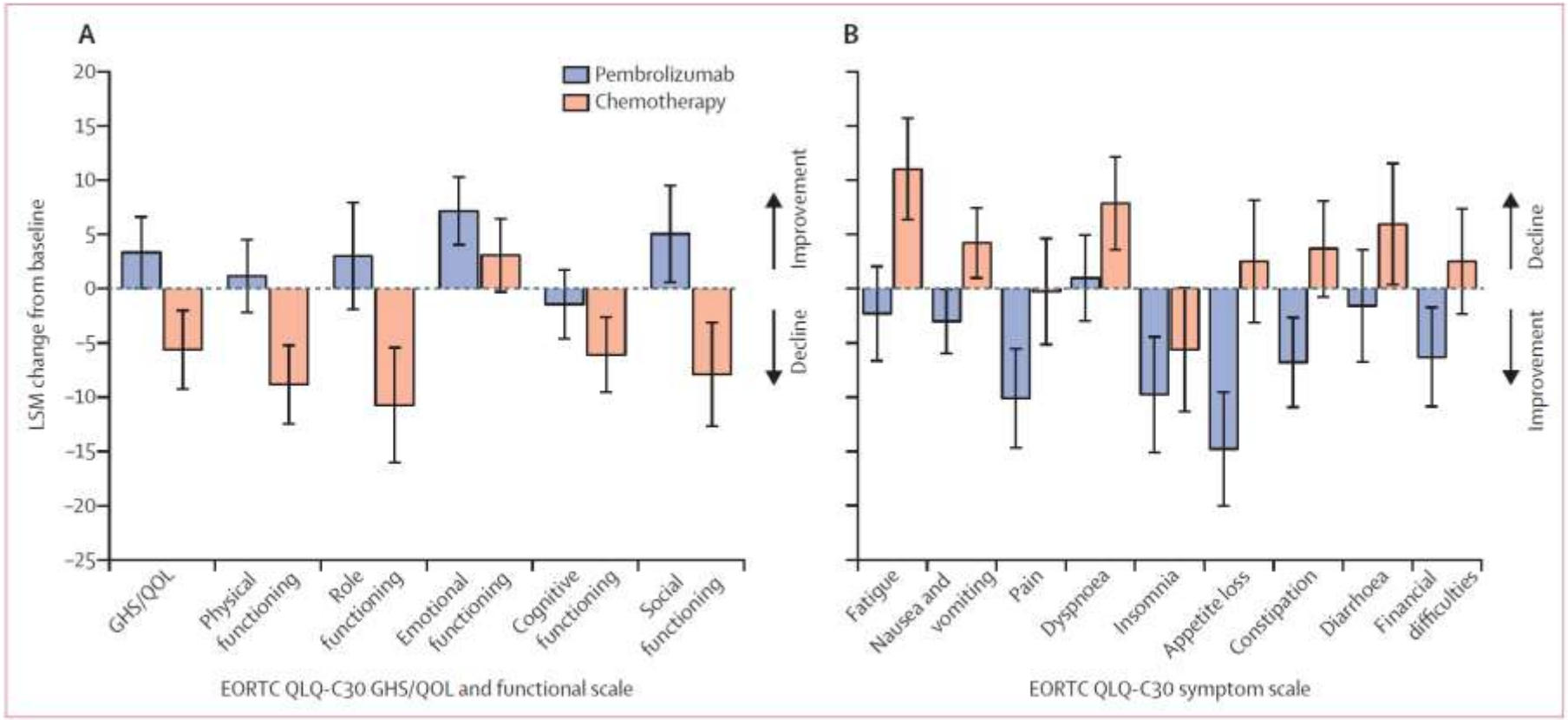
T. André, K.-K. Shiu, T.W. Kim, B.V. Jensen, L.H. Jensen, C. Punt, D. Smith, R. Garcia-Carbonero, M. Benavides, P. Gibbs, C. de la Fouchardiere, F. Rivera, E. Elez, J. Bendell, D.T. Le, T. Yoshino, E. Van Cutsem, P. Yang, M.Z.H. Farooqui, P. Marinello, and L.A. Diaz, Jr., for the KEYNOTE-177 Investigators*



Health-related quality of life in patients with microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer treated with first-line pembrolizumab versus chemotherapy (KEYNOTE-177): an open-label, randomised, phase 3 trial

Lancet Oncol 2021; 22: 665–77

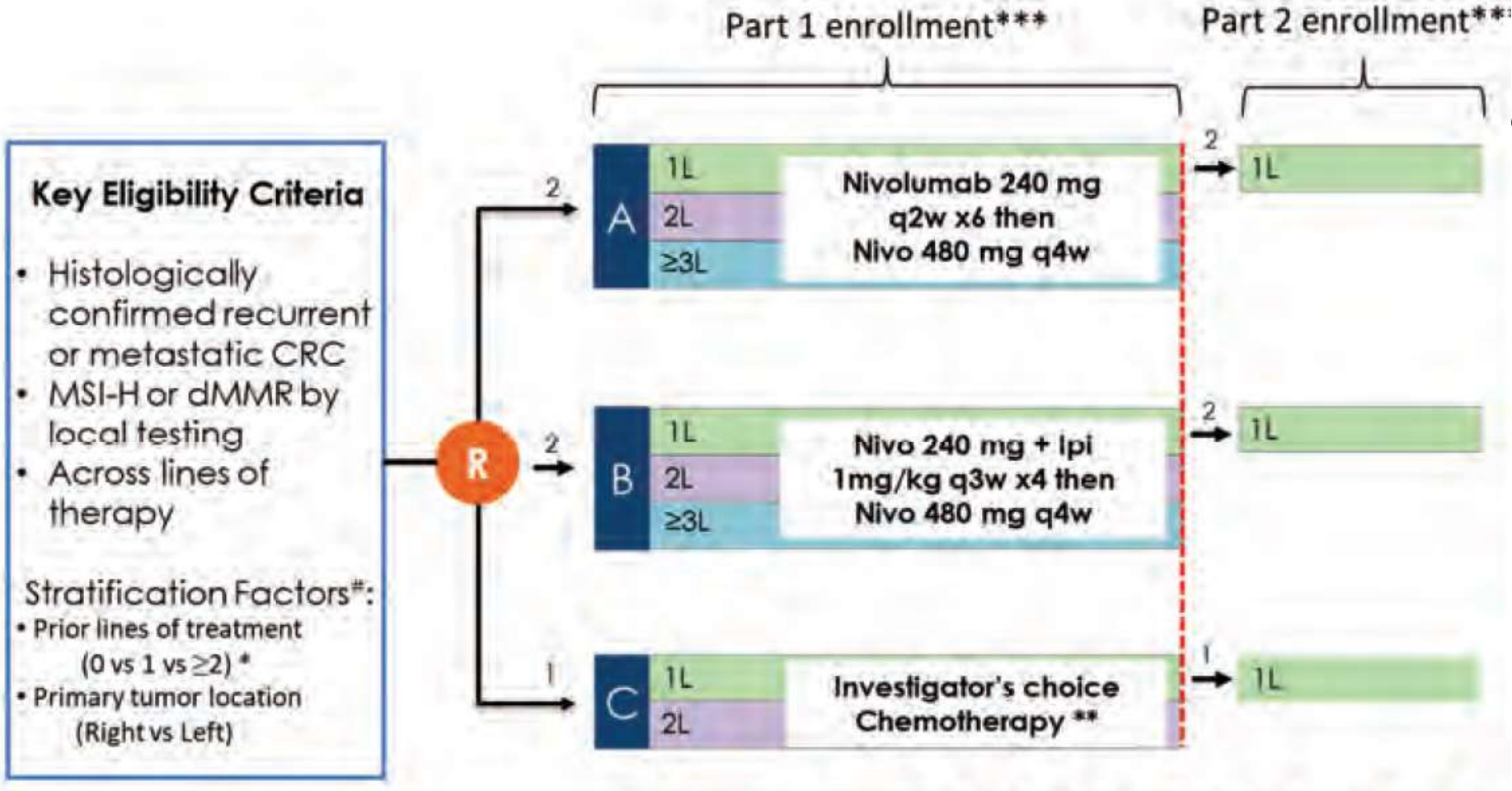
Thierry Andre, Mayur Amonkar, Josephine M Norquist, Kai-Keen Shiu, Tae Won Kim, Benny Vittrup Jensen, Lars Henrik Jensen, Cornelis J A Punt, Denis Smith, Rocio Garcia-Carbonero, Isabel Sevilla, Christelle De La Fouchardiere, Fernando Rivera, Elena Elez, Luis A Diaz Jr, Takayuki Yoshino, Eric Van Cutsem, Ping Yang, Mohammed Farooqui, Dung T Le



A phase 3 study of nivolumab, nivolumab + ipilimumab, or chemotherapy for microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer: CheckMate 8HW

Abstract P-12

Thierry Andre,[1] Eric Van Cutsem,[2] Elena Elez,[3] Jaafar Bennouna,[4] Christelle de la Fouchardiere,[5] Takayuki Yoshino,[6] Lars Henrik Jensen,[7] Guillermo Ariel Mendez,[8] Jin Li,[9] Eray Goekkurt,[10] Sandzhar Abdullaev,[11] Tian Chen,[11] Ming Lei,[11] Sara Lonardi[12]



The NEW ENGLAND JOURNAL of MEDICINE

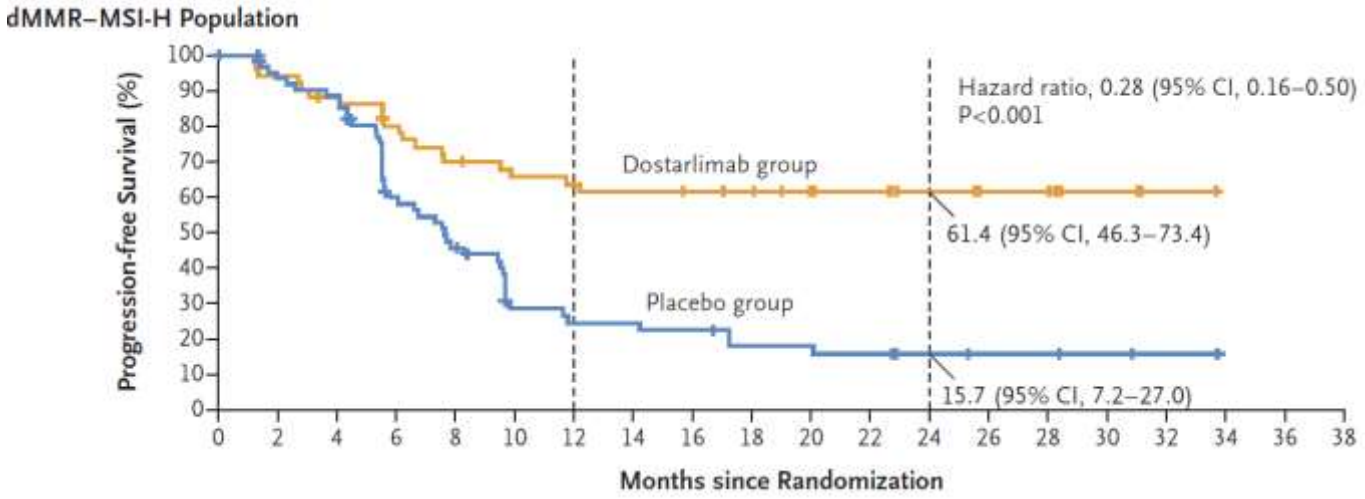
ORIGINAL ARTICLE

Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer

M.R. Mirza, D.M. Chase, B.M. Slomovitz, R. dePont Christensen, Z. Novák, D. Black, L. Gilbert, S. Sharma, G. Valabrega, L.M. Landrum, L.C. Hanker, A. Stuckey, I. Boere, M.A. Gold, A. Auranen, B. Pothuri, D. Cibula, C. McCourt, F. Raspagliesi, M.S. Shahin, S.E. Gill, B.J. Monk, J. Buscema, T.J. Herzog, L.J. Copeland, M. Tian, Z. He, S. Stevens, E. Zografos, R.L. Coleman, and M.A. Powell, for the RUBY Investigators*

CONCLUSIONS

Dostarlimab plus carboplatin–paclitaxel significantly increased progression-free survival among patients with primary advanced or recurrent endometrial cancer, with a substantial benefit in the dMMR–MSI-H population. (Funded by GSK; RUBY ClinicalTrials.gov number, NCT03981796.)



Standard immunotherapy to dMMR in Denmark

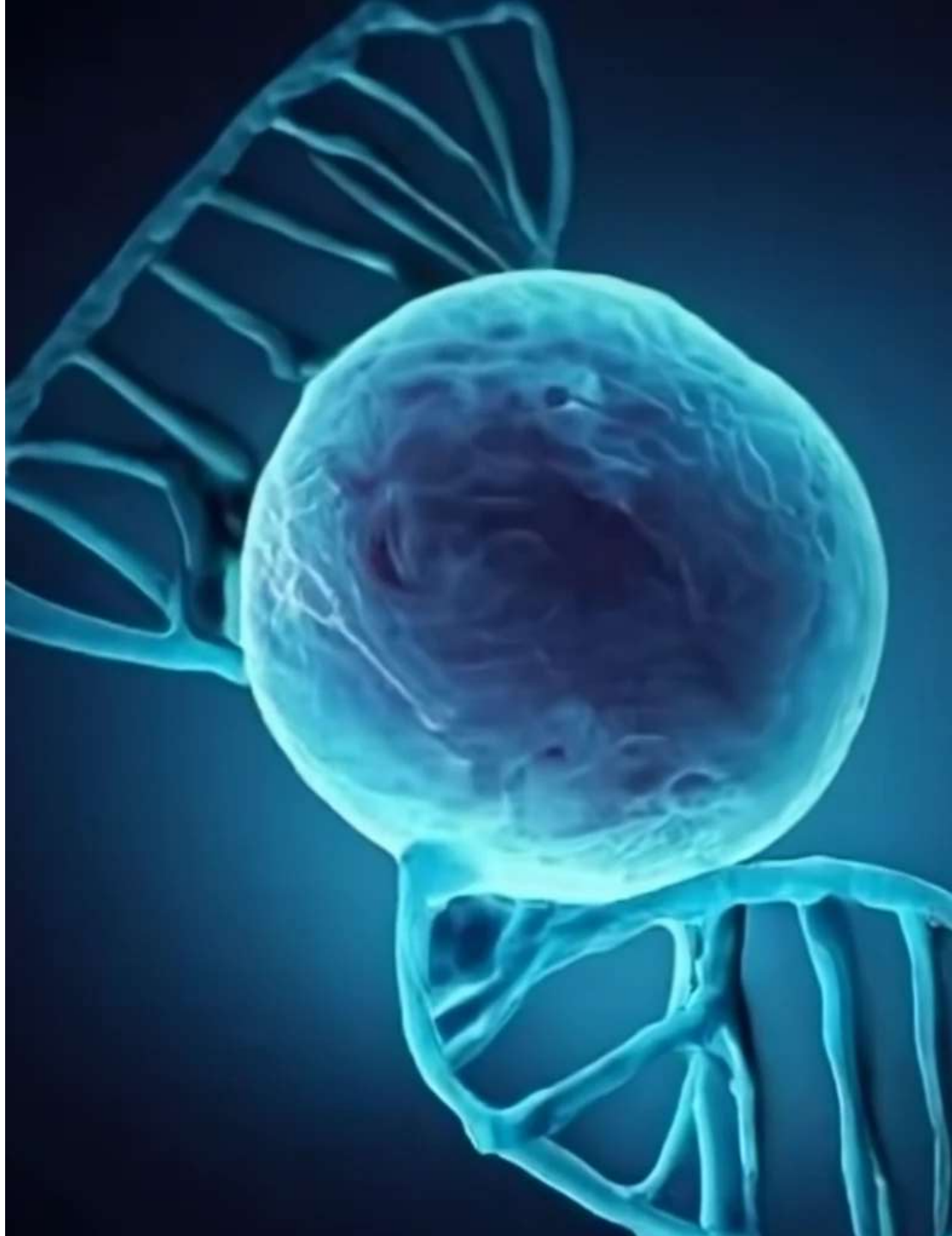
- Not generally approved across histologic subtypes
- Pembrolizumab to dMMR/MSI colorectal cancer, metastatic, first line
- Dostarlimab to platinum resistant, metastatic endometrial cancer – new evaluation underway

Genomic Profiling Workflow

- **Identification of Need**
  - Unsuccessful standard treatment
  - Consideration for genomic profiling
- **Informed Consent**
  - Info on genomic analyses, somatic and hereditary aspects, and consent
- **Biopsy**
  - Tissue sample collection including a parallel sample for standard histopathology
- **WES and RNAseq – or targeted**
  - Whole Exome Sequencing and RNA Sequencing
  - If fresh tissue not available consider archival tissue and a panel e.g. TSO500
- **Data Analysis**
- **National Tumor Board Review**
  - Expert recommendations, including ProTarget, other protocols or recommendation for targeted therapy
- **Potential Targeted Treatment discussed with patient**

ProTarget

- Genomic profiling in all oncology centeres in Denmark
- The trial is designed similar to
  - Dutch DRUP
  - ASCO TAPUR trials
  - - and is a partner in the Nordic Precision Cancer Medicine Trial Network



STUDY PROTOCOL Open Access

ProTarget: a Danish Nationwide Clinical Trial on Targeted Cancer Treatment based on genomic profiling – a national, phase 2, prospective, multi-drug, non-randomized, open-label basket trial

Tina Kringelbach[1], Martin Højgaard[1], Kristoffer Rohrberg[1], Iben Spanggaard[1], Britt Elmedal Laursen[2], Morten Ladekarl[3], Charlotte Aaquist Haslund[3], Laurine Harsløf[1], Laila Belcaid[1], Julie Gehl[4,5], Lise Søndergaard[4], Rikke Løvendahl Eefsen[6], Karin Holmskov Hansen[7], Annette Raskov Kodahl[7,8], Lars Henrik Jensen[9], Marianne Ingerslev Holt[10], Trine Heide Oellegaard[11], Christina Westmose Yde[12], Lise Barlebo Ahlborn[12] and Ulrik Lassen[1*]

Kringelbach *et al. BMC Cancer* (2023) 23:182
https://doi.org/10.1186/s12885-023-10632-9

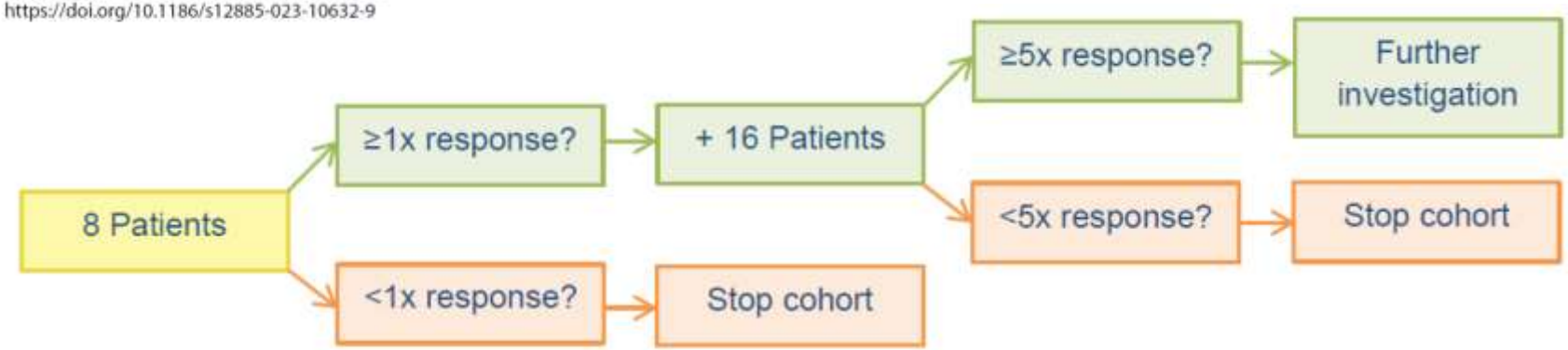


Figure 3: Number of patients per cohort. Cohorts are defined by histologic tumor type, molecular tumor profile and study drug.

Table 4 ProTarget Drugs and Acceptable Molecular Alterations

Drug	Acceptable Genomic Alterations[ab]	E
Alectinib	*EML4-ALK* fusions or mutations, *ROS1* fusions	N
Atezolizumab	MSI high	N
	POLE mutations: R150X, P286R, P286H, S297F, Y298fs, F367S, V411L, L424V, P436R, V437M, S459F, R573L, E597K, R665W, L698fs, R762W, R793C, K1008N, T1052M, R1111Q, L1235I, V1368M, R1519C, P1547S, R1826W, R1879C, Y1889C, S1892N, A1967V, A2213V, A2243T	
	POLD1 mutations: W79L, P112fs, A930fs, N247I, R352C, Q461H, S478N, A864T, E1105D	
	TMB ≥10 mut/mb	
Avelumab	MSI high	N
	POLE mutations: R150X, P286R, P286H, S297F, Y298fs, F367S, V411L, L424V, P436R, V437M, S459F, R573L, E597K, R665W, L698fs, R762W, R793C, K1008N, T1052M, R1111Q, L1235I, V1368M, R1519C, P1547S, R1826W, R1879C, Y1889C, S1892N, A1967V, A2213V, A2243T	
	POLD1 mutations: W79L, P112fs, A930fs, N247I, R352C, Q461H, S478N, A864T, E1105D	
	TMB ≥10 mut/mb	

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Several options

Changes over time

Find a way for the individual patient