Global Access to Cancer Immunotherapy: Closing the Gaps

Challenges in checkpoint blockade clinical trial design and execution. Site readiness for immunotherapy – Eastern European perspective.

December 9th, 2020

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Society for Immunotherapy of Cancer

INTRODUCTION

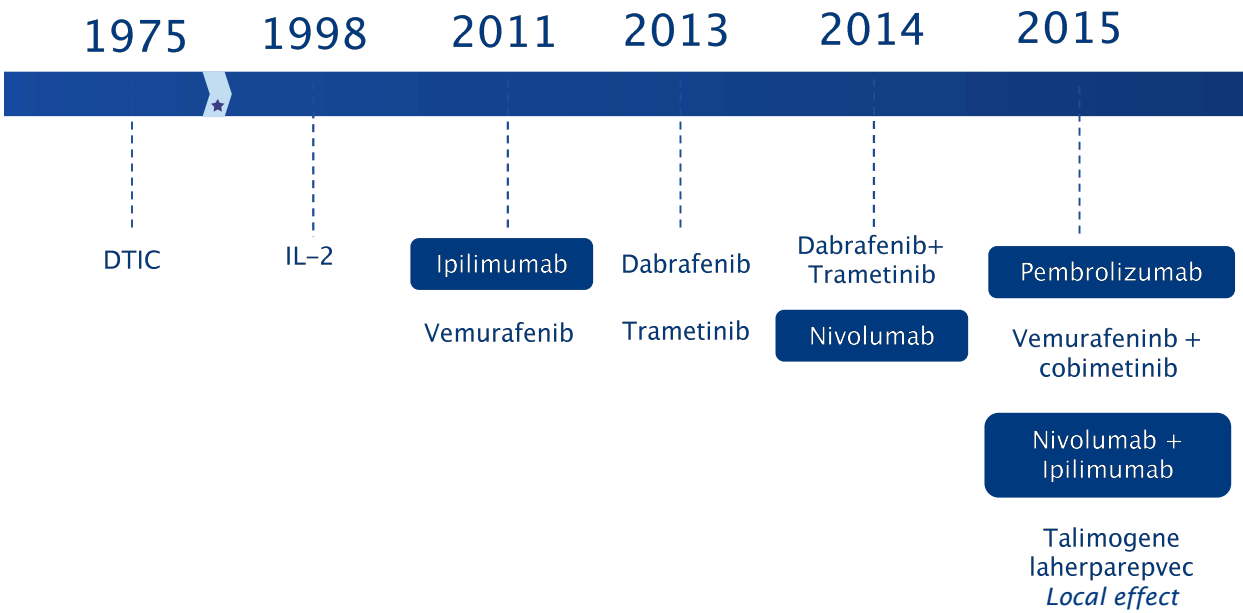
This meeting coincides with the 10th anniversary of the publication of data indicating the efficacy of ipilimumab in metastatic melanoma
(Hodi FS. et al. Improved survival with ipilimumab in patients with metastatic melanoma. N Engl J Med 2010;363:711-23)

Since then, a number of additional check-point inhibitors have been proven to bring OS and other clinical benefits in melanoma and at-least twelve other solid tumors and hematologic cancers.

Patient access to checkpoint blocking agents remains unequal and often depends on the income status of their country of origin.

REGIONAL DISPARITIES

FDA-Approved Agents for Unresectable / Advanced Melanoma



Eastern Europe

2020

All exist under the treatment guidelines, however, they are not accessible under national healthcare

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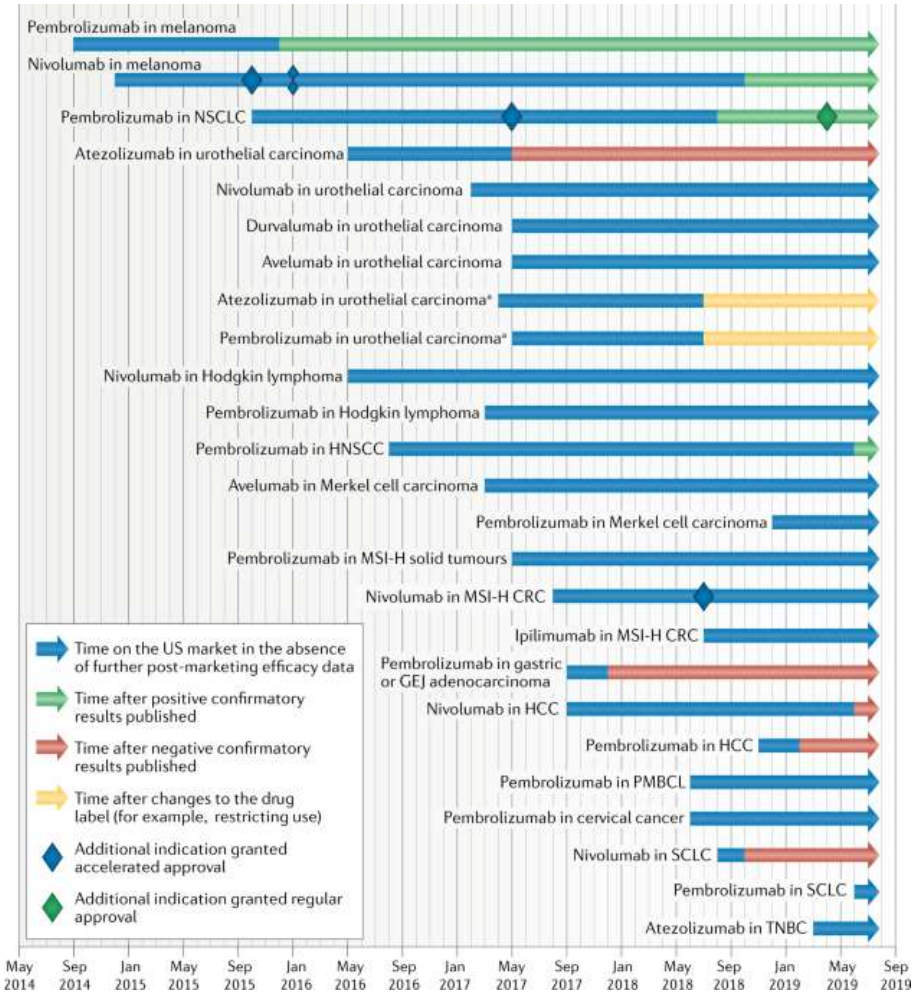
Source:
http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm (46).

A REALITY CHECK OF APPROVAL OF CPI

Melanoma and NSCLC are the two first and most established indications for CPI to date



Source: A reality check of the accelerated approval of immune-checkpoint inhibitors *Nature Reviews Clinical Oncology* **volume 16,** pages656-658(2019)

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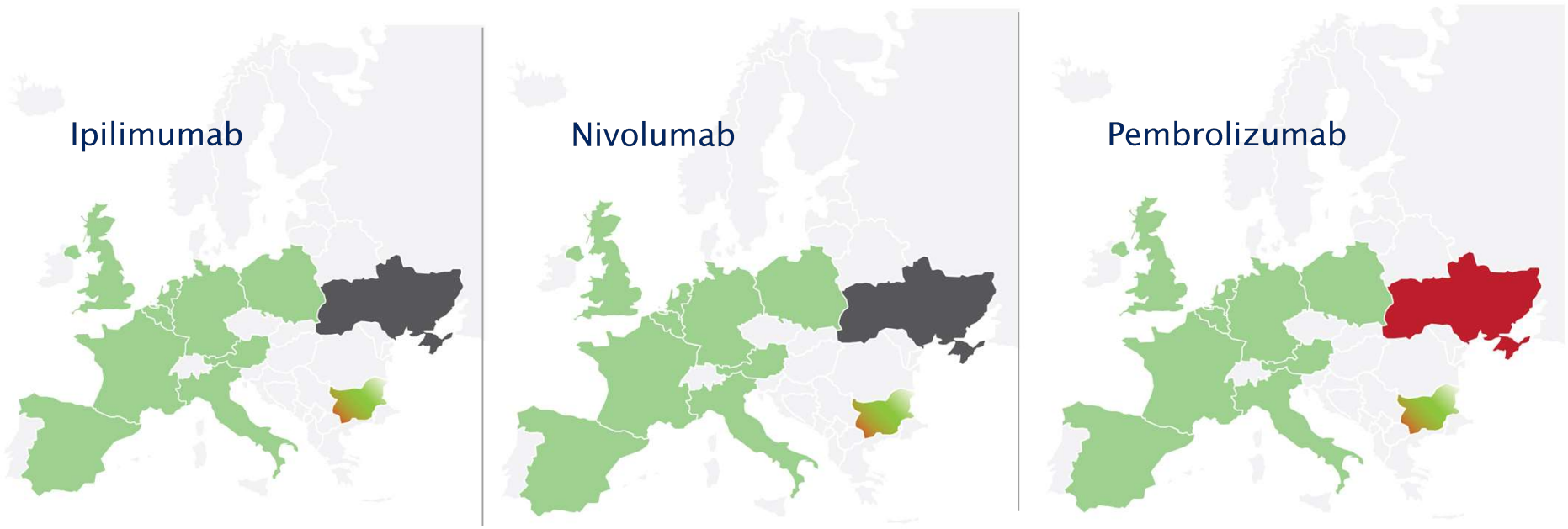
ACCESS TO CPI TREATMENT (MELANOMA, LUNG)



Not Reimbursed
Reimbursed
Not registered

Access to innovative treatment (immunotherapy) in registered indications

WE: high low:EE

EXEMPLARY RANGE OF CPI REIMBURSEMENT

	Ipilimumab	Pembrolizumab – melanoma	Pembrolizumab – NSCLC
 Bulgaria	Monotherapy for the treatment of advanced (inoperable or metastatic) melanoma in adults Combination therapy with nivolumab for the treatment of advanced (unresectable or metastatic) melanoma in adults	○ Monotherapy for the treatment of advanced (inoperable or metastatic) melanoma in adults; ○ Monotherapy for the adjuvant treatment of adults with stage III melanoma and lymph node involvement in which complete resection has been performed.	○ Monotherapy for the treatment of first-line metastatic non-small cell lung cancer (NSCLC) in adults whose tumors express PD-L1 with a ≥ 50% proportional tumor score (TPS), without EGFR or ALK positive tumor mutations; ○ For the treatment of locally advanced or metastatic NSCLC in adults whose tumors express PD-L1 with ≥ 1% TPS and who have received at least one prior chemotherapy regimen. Patients with EGFR or ALK positive tumor mutations should also have received targeted therapy prior to treatment with nivolumab; ○ In combination with pemetrexed and platinum chemotherapy for the treatment of first-line metastatic non-squamous NSCLC in adults whose tumors do not have EGFR or ALK positive mutations ○ For the treatment of first-line metastatic squamous non-small cell lung cancer (NSCLC) in adults in combination with carboplatin and paclitaxel or in combination with carboplatin and nab-paclitaxel;
 Ukraine	Not registered	No reimbursement	Not registered

CONCLUSION

- Despite a 10-year history of overall survival and other clinical benefits, patient access to checkpoint blocking agents remains limited.
- The authors estimate that in the entire region of Southern and Eastern Europe, there are still double-digit percentages of patients without the access to first-line therapies recommended by the European guidelines (ESMO, EDF/EORTC/EADO)*
- In addition, it seems reasonable to still say that almost one third of all metastatic melanoma patients do not have access to innovative medicines *
- The COVID-19 pandemic will constitute an additional factor limiting the resources in global healthcare

Source: * CDDF Multiple-staheholder workshop: Access to innovative oncology drugs in Europe, 7-8 September, 2017, Professor Lidija Kandolf Sekulovic

CASE STUDIES

placement of clinical trials

ACCESS TO CPI NAÏVE AND POST CPI POPULATIONS

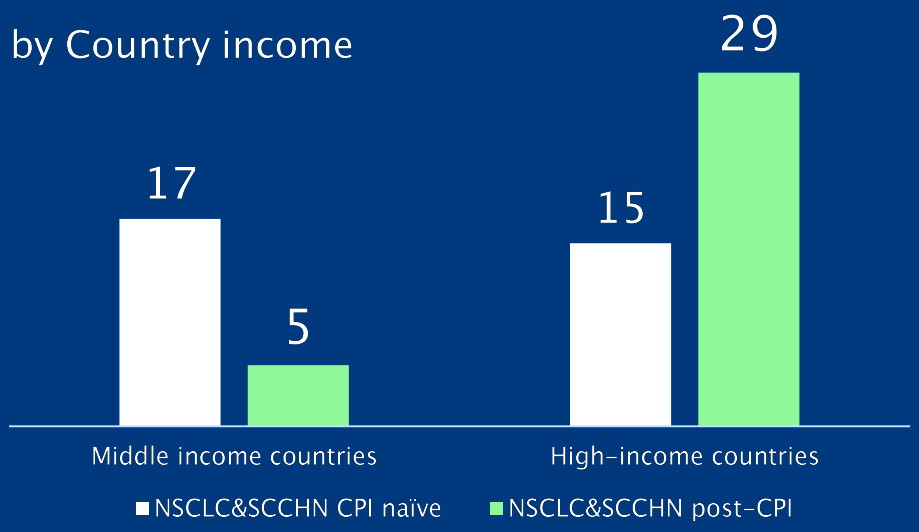
Case study 1

Investigational therapy: a dual checkpoint blockage (anti-PD-1, anti-LAG 3)

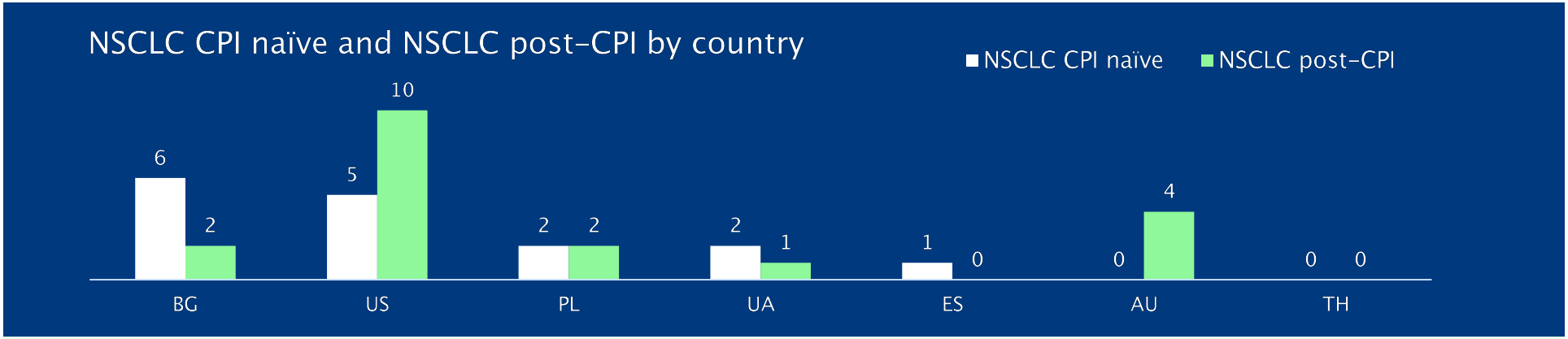
Indications: basket study with nine different indications, including CPI naïve and pre-treated HNSCC and NSCLC

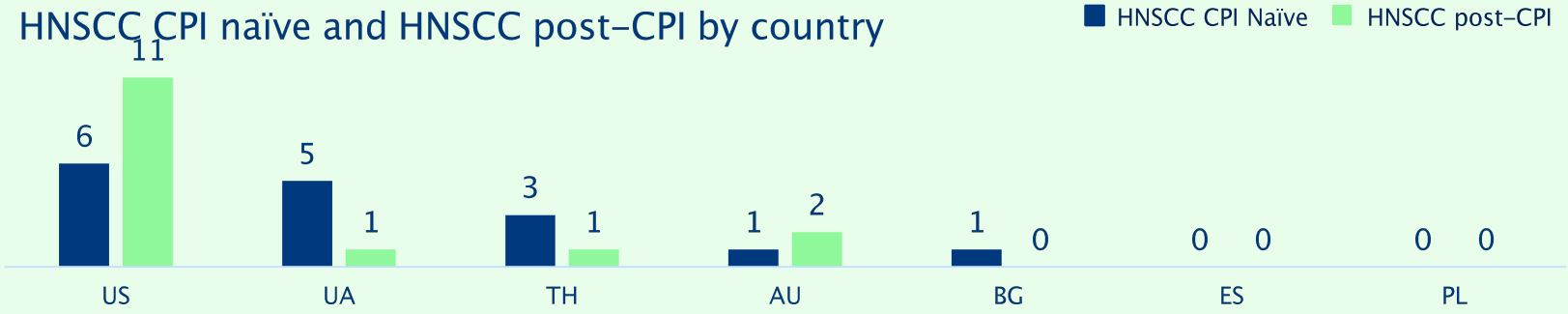
Timeframe: 2019/early 2020

Context of data presentation: indications of regions with still problematic access to CPI in established indications



NAÏVE VS POST-CPI COHORTS SPLIT BY COUNTRY





Middle-income European countries continue to have low patient access to checkpoint blocking agents and thus, can continue to be considered for first-line immunotherapy trial designs.

ACCESS TO CPI IN HNSCC

Case study 2

Investigational therapy: immunomodulation in addition to checkpoint blockage

Indications: r/m HNSCC, first line treatment

Timeframe: data accessed in September 2020

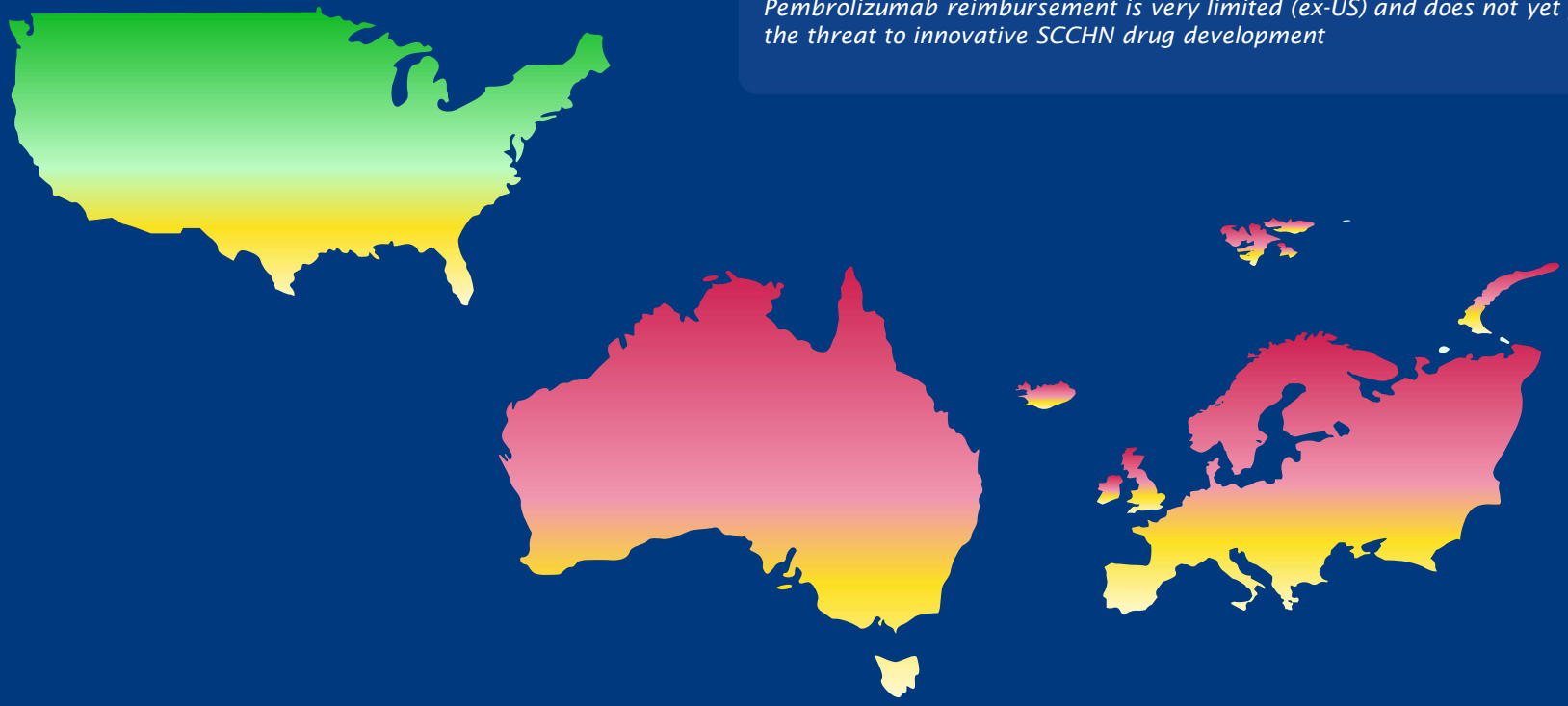
Context of data presentation: slow update of CPI market access despite publishing of confirmatory efficacy results

APPROVED USE OF PEMBROLIZUMAB IN SCCHN

Region	*Approved Indication
United States	• In combo with platinum and FU for first-line treatment in patients with metastatic or unresectable, recurrent disease • As a single agent for the first-line treatment in patients with metastatic or unresectable, recurrent disease whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] • As a single agent for patients with recurrent or metastatic disease with disease progression on or after platinum-containing chemotherapy.
Europe	• As a single agent or in combination with platinum and FU for the first-line treatment in patients with metastatic or unresectable, recurrent disease whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] • As monotherapy in patients with recurrent or metastatic disease whose tumors express PD-L1 with a ≥ 50% TPS and progressing on or after platinum-containing chemotherapy
Australia	• Monotherapy in patients with recurrent or metastatic disease with progression on or after platinum-containing chemotherapy

*Approving Health Authorities: US = FDA; Europe = EMA; Australia = TGA

PEMBROLIZUMAB ACCESS IN SCCHN



Pembrolizumab reimbursement is very limited (ex-US) and does not yet pose the threat to innovative SCCHN drug development

Despite break-thru data published in connection with ASCO 2019 and 2020, HNSCC patient access to immunotherapy in the first line setting is sparse and will unlikely evolve, particularly in the Southern and Eastern European countries.

CANCER IMMUNOTHERAPY RESEARCH

Region	Number of CTs
United States	569
Germany	111
Poland	61
Ukraine	32

Of note, Ukrainian centers did not participate in several important immunotherapy studies presented on ESMO-2020 (IMpassion131, KEYNOTE-590, KEYNOTE-048, KEYNOTE-054).

Search criteria: pembrolizumab
Other terms: Keytruda, MK-3475, and Lambrolizumab
Trial status: recruiting, not yet recruiting,

Eastern and Southern Europe still face challenges in accessing checkpoint blockades.

This creates an opportunity for drug developers to place studies in middle-income countries, not only for the economic benefit, but also in respect to ethical mandates and the general emphasis on putting treatments closer to patients.

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