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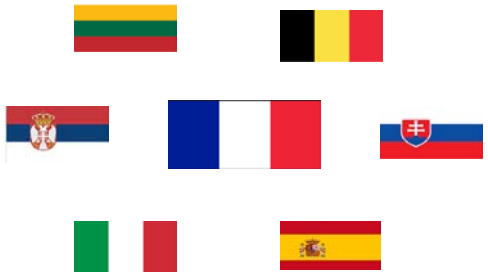

# WP9 – Current state of play

Govermental Board – 09 October 2019

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# WP9 TASKS AND GOALS

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## INNOVATIVE THERAPIES IN CANCER

1) **Map existing guidelines** and reference frameworks regarding the use of immunotherapies in clinical practices and identify potential off-label use

- Promote the proper use of these innovative treatments
- Spur coordination across institutions, professionals and Member States

2) Identify and validate predictive **biomarkers** for response, resistance or toxicity

- Better identification of responders or non responders

3) Predict impact of forthcoming innovative treatments with **horizon scanning** activities

- Anticipation of new therapies, their associated costs and their place in the therapeutic strategy

4) Identify tools that could be implemented in Europe for **real-life monitoring** of innovative treatments

- Provide guidance regarding the assessment of innovative therapies in real-life setting



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# WP9 SCOPE

- Innovative therapies against cancer
  - Focus on innovative immunotherapies
    - Checkpoint inhibitors
    - CAR-T cells

**OVERVIEW OF THE TYPES OF CANCERS FOR WHICH CHECKPOINT INHIBITORS AND CAR-T CELLS HAVE (AT LEAST) ONE APPROVED THERAPEUTIC INDICATION IN THE EUROPEAN UNION (August 2018)**

| | CHECKPOINT INHIBITORS | | | | |
|---|---|---|---|---|---|
| | anti-CTLA-4 | anti-PD-1 | | anti-PD-L1 | |
| Cancer types* | Ipilimumab (Yervoy®) | Nivolumab (Opdivo®) | Pembrolizumab (Keytruda®) | Avelumab (Bavencio®) | Atezolizumab (Tecentriq®) |
| Melanoma | 2011 | June-15 | July-15 | | |
| Non-small cell lung cancer | | Oct-15 | Aug-16 | | Sept-17 |
| Renal cell carcinoma | | Apr-16 | | | |
| Classical Hodgkin's lymphoma | | Nov-16 | May-17 | | |
| Squamous head and neck cancer | | Apr-17 | | | |
| Urothelial carcinoma | | June-17 | Aug-17 | | Sept-17 |
| Merkel cell carcinoma | | | | Sept-17 | |

| | CAR-T CELLS | |
|---|---|---|
| Cancer types | Tisagenlecleucel (Kymriah®) | Axicabtagene ciloleucel (Yescarta®) |
| B-cell acute lymphoblastic leukaemia (ALL) | Aug-18 | |
| large B-cell lymphoma | Aug-18 | Aug-18 |



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# WP9 – TASK 1

Clinical practice guidelines and reference frameworks related to the use of immunotherapies

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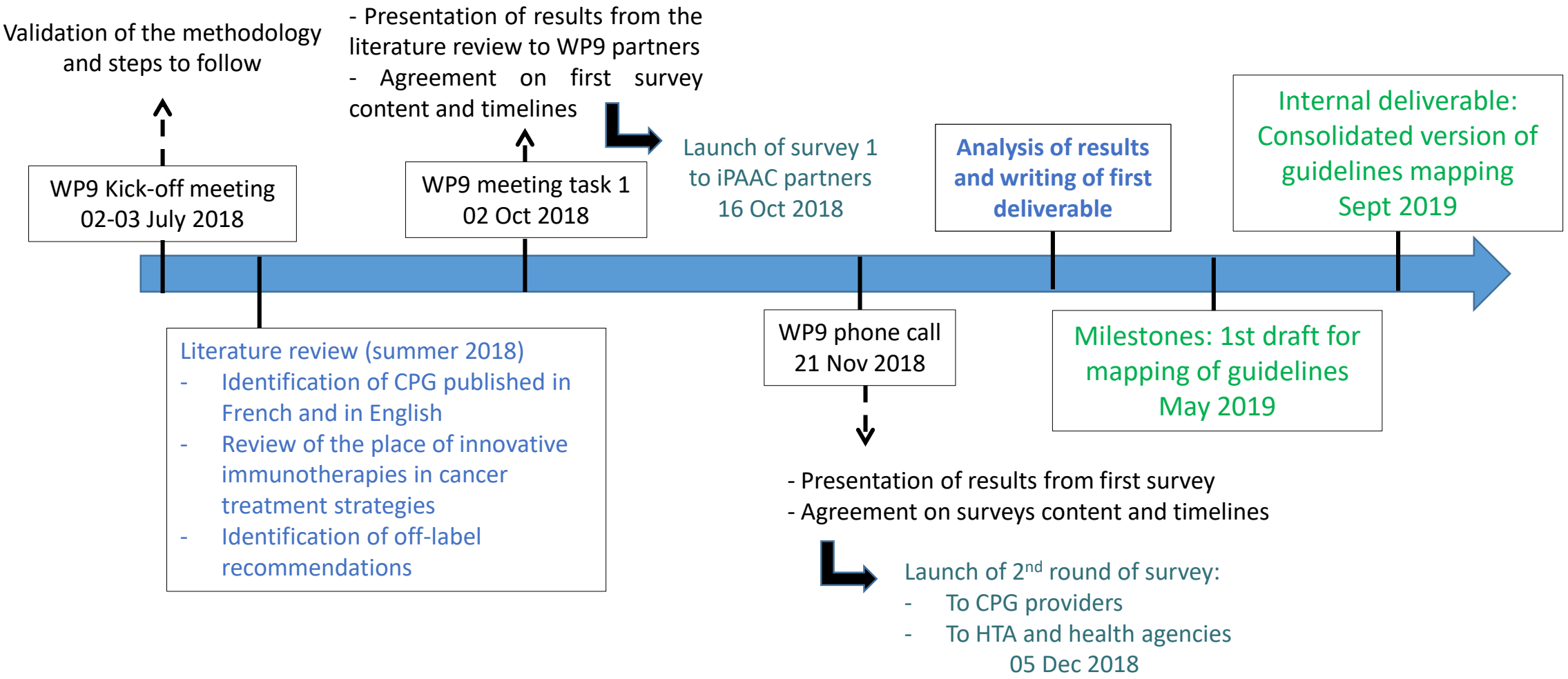
# TIMELINES / MILESTONES TASK 1



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# STRUCTURE OF THE WORK FOR WP9 TASK 1: 2 DELIVERABLES

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1. Innovative immunotherapies in clinical practice guidelines
    - Mapping of clinical practice guidelines
    - Place of innovative immunotherapies within guidelines
    - Off-label recommendations: why, from who, how?
2. Reference frameworks linked to access to innovative immunotherapies
    - Comparison of access in terms of reimbursement & restrictions of uses
    - Mapping of programs/reference frameworks enabling early access to innovative immunotherapies for unapproved indication



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# INNOVATIVE IMMUNOTHERAPIES IN CLINICAL PRACTICE GUIDELINES

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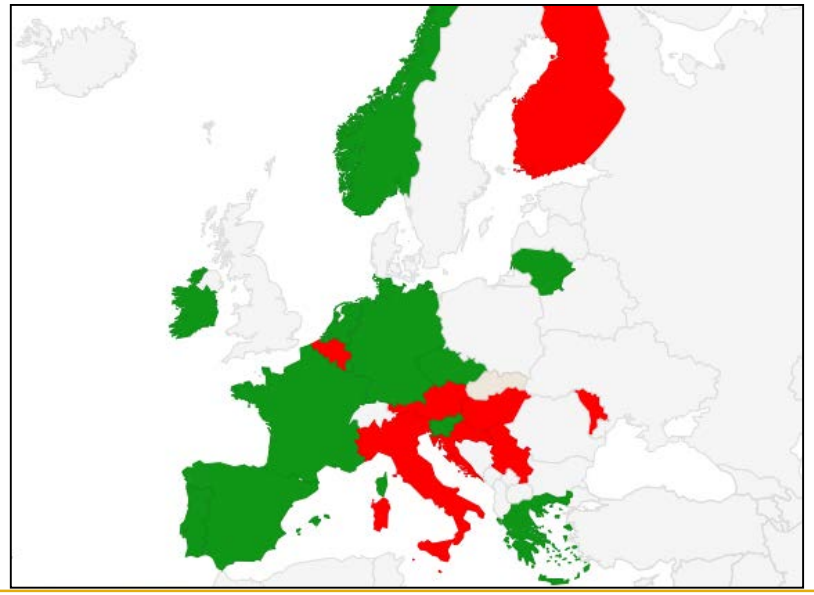
- Most of the European countries have at least one national or regional organization in charge of writing clinical practices guidelines related to oncology
- Only half of the countries (12/23, 52%) had included innovative immunotherapies in the treatment strategy in at least one clinical practice guideline related to oncology



- Some ideas were suggested to improve timelines for production and update of guidelines such as:
  - support from robust methodology,
  - standardized operational procedures,
  - dedicated in-house staff with methodological expertise,
  - reduction of the scope of guidelines,
  - strengthen the training on methodological approach for medical doctors and experts involved in the production of guidelines,
  - increasing financial support,
  - Strengthen collaboration, especially for rare types of cancers and therapeutic areas where no specific society exists,
  - implementation of endorsement systems.



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# REMAINING CHALLENGES

- Defining the best place of innovative therapies in cancer treatment strategies, especially when comparison data are missing
  - The experts solicited thought for a large majority of them (90%) that a public fund financing studies comparing innovative immunotherapies between them could be helpful to better define the place of innovative therapies in cancer treatment strategies.
- Acceptability of off-label recommendations in clinical practice guidelines varies across experts
- Improve the visibility of national guidelines at the European level
  - Publication in local langage / barrier langage
  - Only few are referenced in PubMed
  - Creation of a repository platform?
- Improve timelines for production and update of guideline



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# COMPARISON OF ACCESS TO INNOVATIVE IMMUNOTHERAPIES IN EUROPEAN UNION

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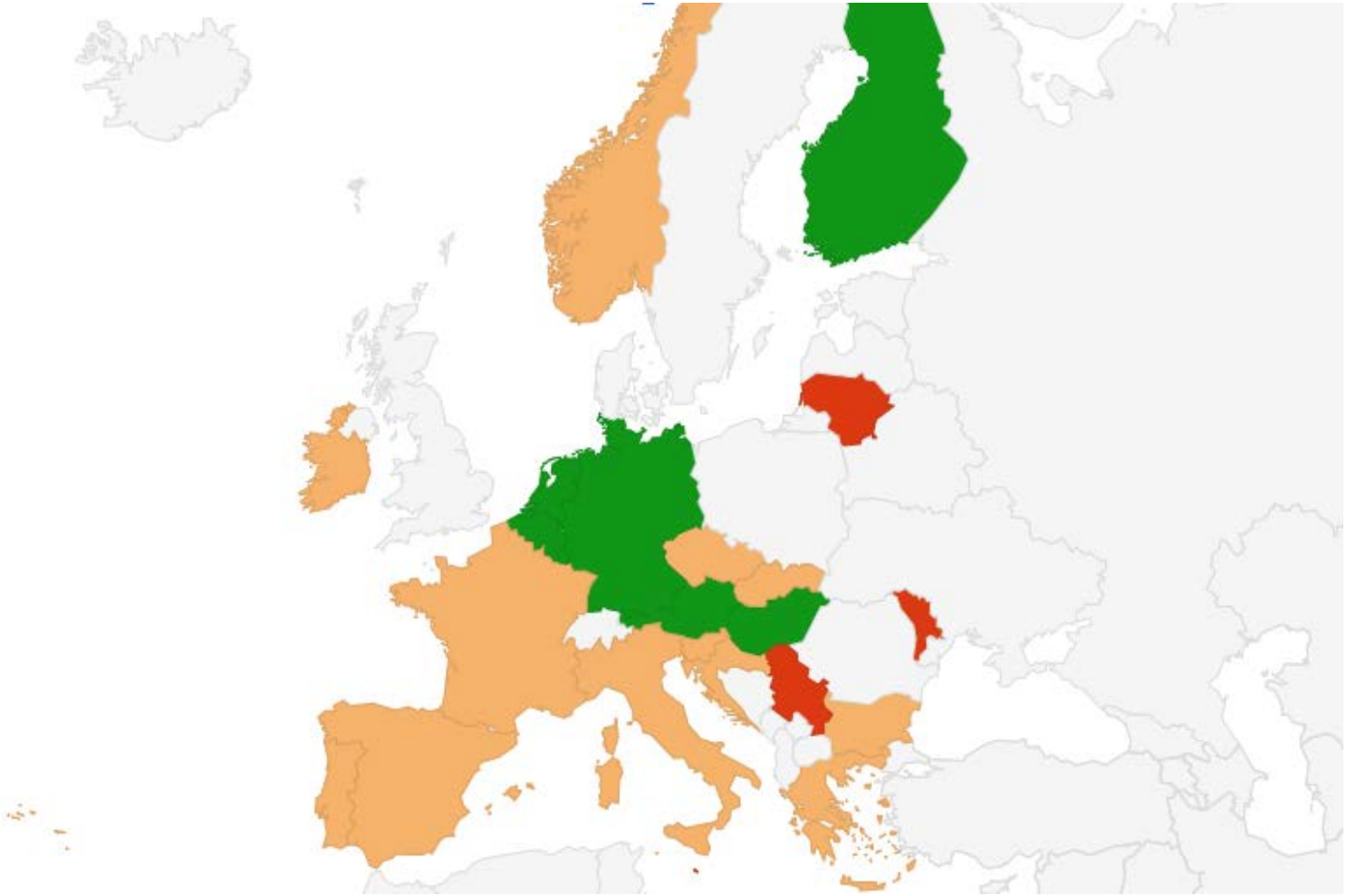

High access (≥ 15 indications reimbursed with no restrictions compared to EU MA)

Moderate access

No access or very limited

*As per data collected in October 2018*
*For Lithuania, data were collected for lung cancer only*



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# ACCESS TO INNOVATIVE THERAPIES: COMPARISON OF INDICATIONS

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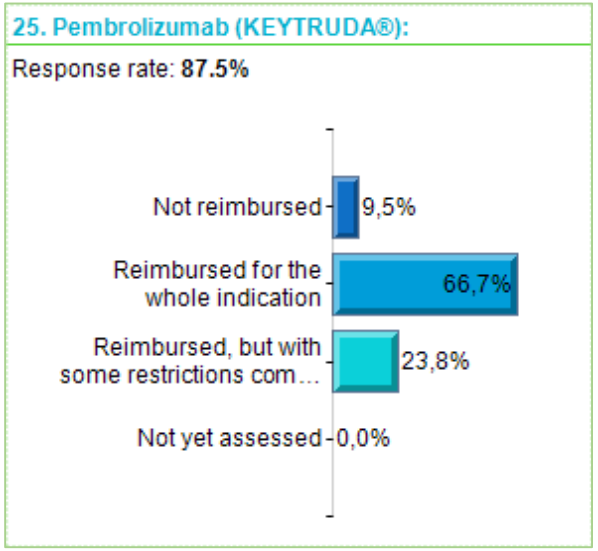
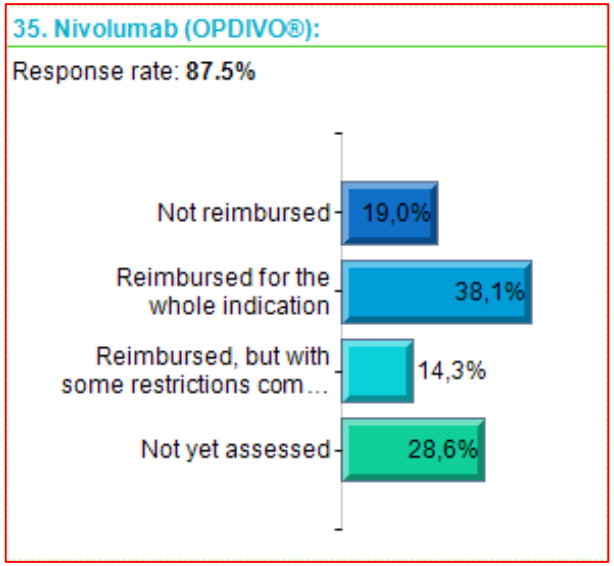
*Keytruda as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.*




*OPDIVO as monotherapy is indicated for the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy.*

- Three main factors leading to restrictions of reimbursement / access of innovative therapies were identified:
  - low level of scientific and medical evidence supporting marketing authorization;
  - missing direct comparison data with alternative therapies;
  - high costs of innovative immunotherapies.



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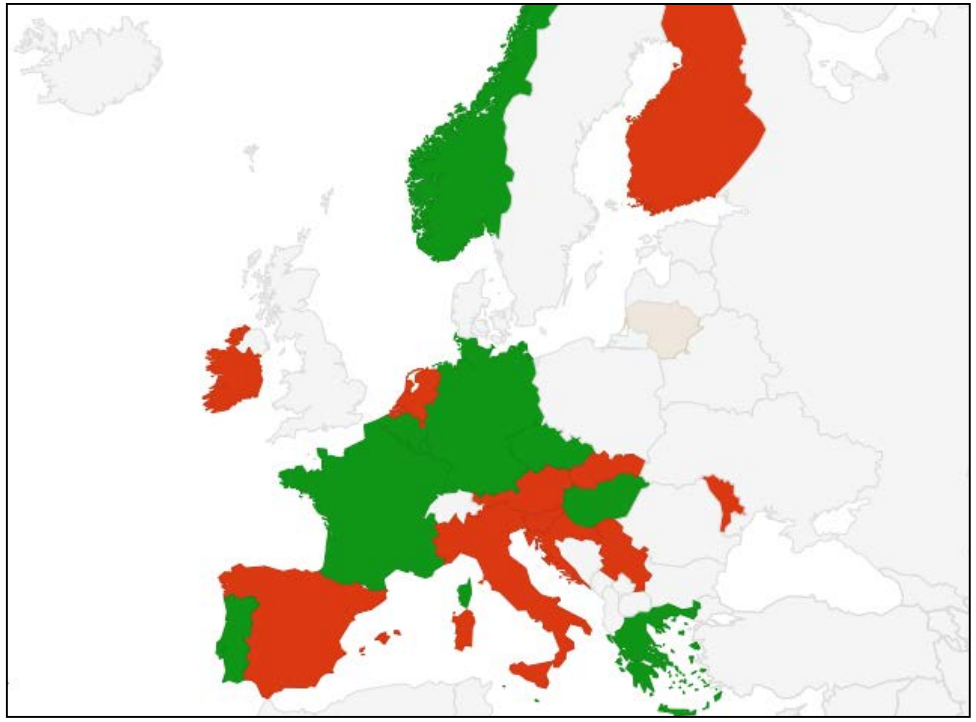
# EARLY ACCESS PROGRAMS

- About half of the countries (10/22, 45%) mentioned that they have an existing program enabling early access to innovation therapies against cancer (before marketing authorization or before extension of indication).



*Note: N = 22 countries*
*(no reply received from Lithuania on this topic)*

- 80% of the persons who replied that they have an existing early access program in there country were satisfied with the implemented program.
- Strong interactions between the different national and regional agencies and clear defined pathways and juridical frameworks are necessary.



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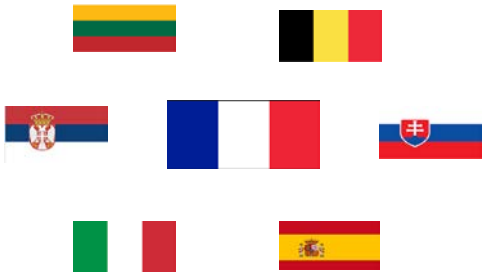

# WP9 – TASK 2

Biomarkers

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# BIOMARKERS

- Fully integrated in task 1 & 3
- Main biomarkers identified
    - PD-L1 expression
    - MSI-H
    - TMB
    - BRAF status (conditioning the potential presciption of some anti-PD-1)



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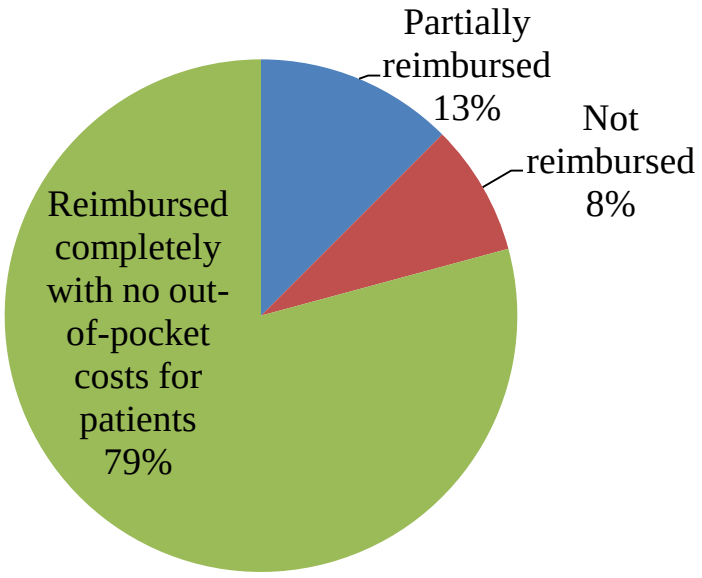
# REIMBURSEMENT OF BIOMARKER EXPRESSION TESTS

- When the prescriptions of immunotherapies are conditioned by the prerequisite of a specific biomarker expression, is the molecular test to assess the biomarker reimbursed in your country?




*Note: For Spain, the reimbursement might varies depending on the region*



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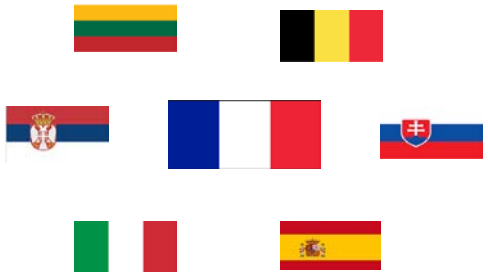

# WP9 – TASK 3

Horizon Scanning Systems

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# ONCOLOGY IN CLINICAL RESEARCH

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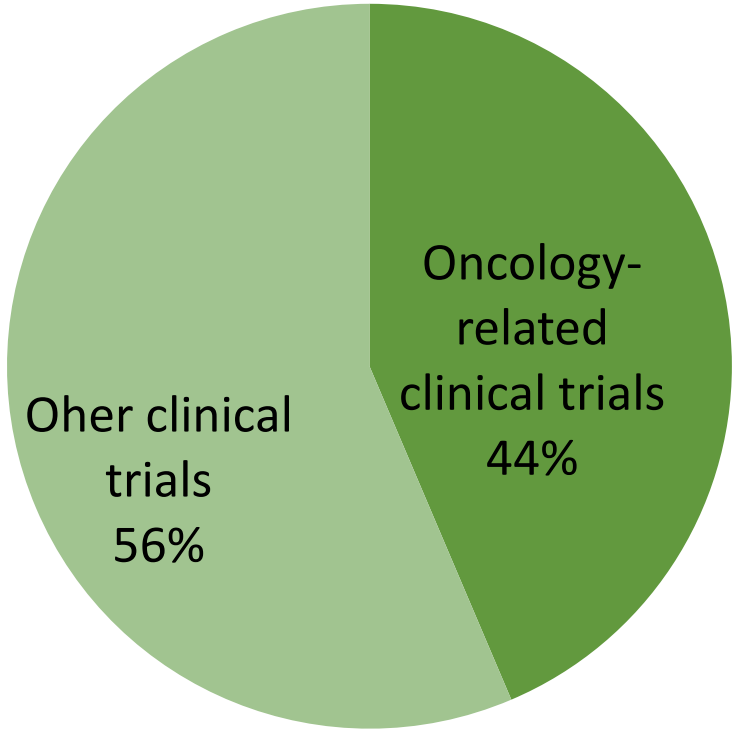
- On 07 December 2018, **127 146 studies** in the field of **oncology** were entered on clinicaltrial.gov
- More than 700 cancer drugs are in late-stage development (IQVIA report - 2018)
- Over one-third of trials are using biomarkers to stratify patients (IQVIA report - 2018)

➔ Considering the importance of oncology in the development of innovative therapies as well as its strong arrival on the market, it is important to consider all specificities that might have these therapies and that might impact horizon scanning methodology




*Source: extraction of data from clinicaltrial.gov (December 2018)*



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# TIMELINES / MILESTONES TASK 3

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WP9 Kick-off meeting
02-03 July 2018

WP9 meeting task 2 & 3
06 March 2019

WP9 meeting task 2 & 3
18 November 2019

April 2020
Internal deliverable regarding
Horizon scanning in Europe

Milestones: 1st draft
November 2019

Preparation of the task
- Literature review
- Meetings with Euroscan, IHSI

Retrospective analysis to evaluate the efficiency of HS in oncology

Review of existing Horizon scanning systems and organizations

eunethta
EuroScan International Network
Canadian Agency for Drugs and Technologies in Health
BeNeLuxA

Identification of key figures and issues associated with innovative cancer therapies

OECD
FDA
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

- Highlight specific features needed in HS systems for
  - cell and gene therapies
  - Biomarkers
- Assessment of inequalities between European Countries



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# WHAT TO EXPECT FOR THE TASK 3 DELIVERABLE

- Get a better understanding on what are horizon scanning systems and what they can be used for;
- Provide concrete examples of systems already implemented with a focus on strengths and weaknesses in the oncology field;
- Highlight potential specific features to be considered in terms of methodology for the identification and for the assessment of impact of innovative therapies in cancer (with a focus on biomarkers and gene and cell therapies)
- Increase the visibility of ongoing European initiatives and collaboration on this thematic
- Increase awareness on methodological tools already existing;
- Assessment of inequalities between European countries in terms of anticipation of new therapies.
- Provide suggestions to decrease inequalities and reinforce collaboration in Europe. For instance, share more HSS outputs like:
  - the list of medicines considered to have a significant clinical impact
  - The list of medicines prioritized by other HTA agencies
  - Difficulties/Specificities that other agencies could have encountered with specific medicines (eg CAR-T cells)



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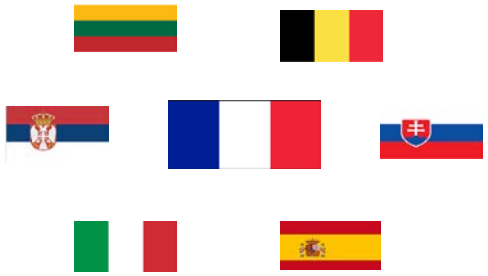

# WP9 – TASK 4

Real-life monitoring of innovative immunotherapies

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# REAL-LIFE MONITORING OF INNOVATIVE IMMUNOTHERAPIES

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- Next meeting: February 25th in Ljubljana
- Focus on specificities to be considered for the real-life monitoring of innovative immunotherapies



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# Any questions/suggestions?

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