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The role of real world data (RWD) in the decision making for the reimbursement of medicines

Τα δεδομένα της καθημερινής κλινικής πρακτικής ως εργαλείο λήψης απόφασης στην Κοινωνική Ασφάλιση

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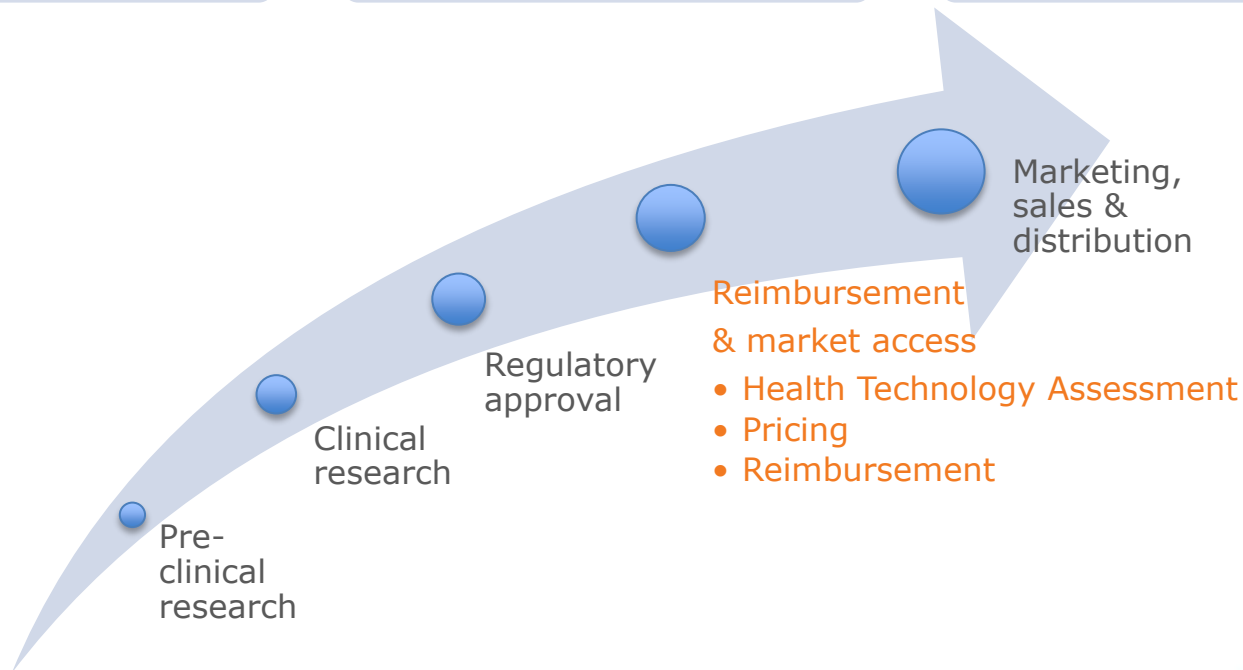
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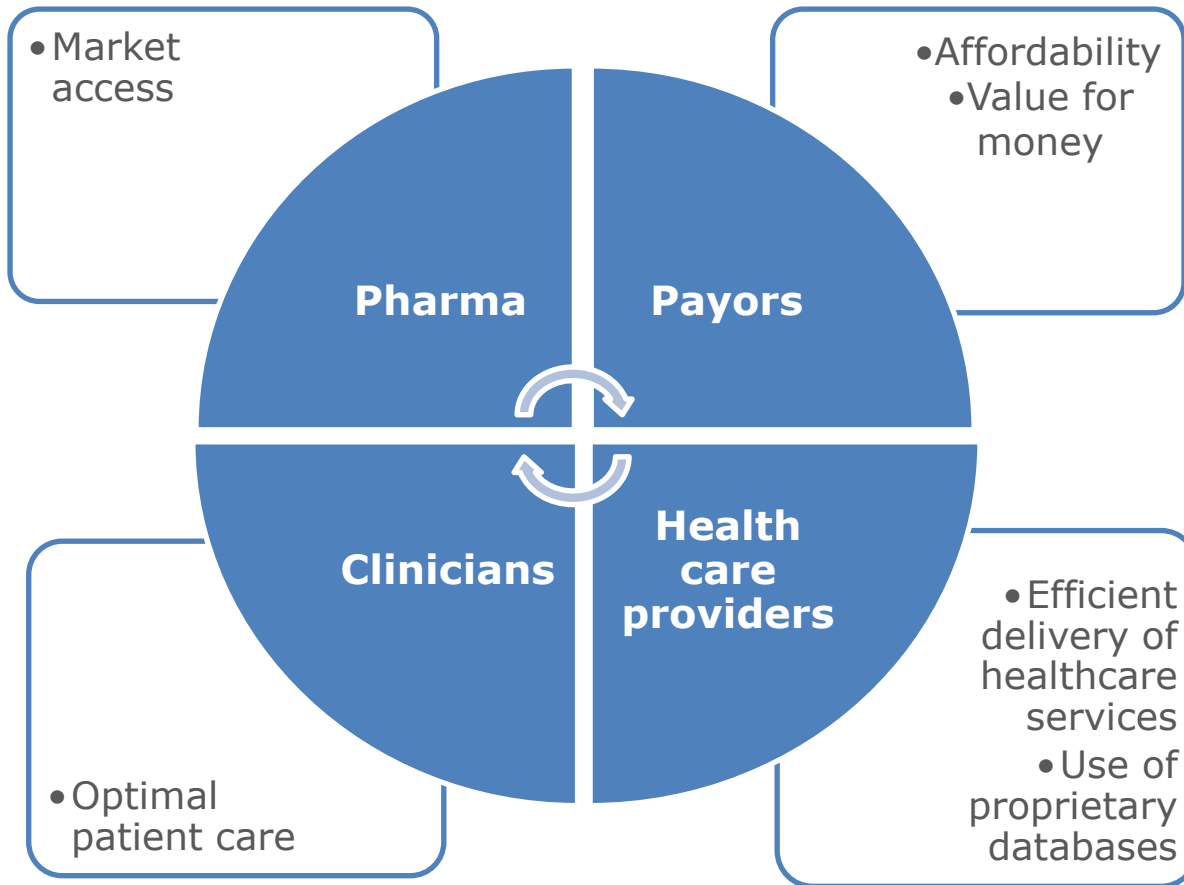


Product development till implementation in healthcare

Different goals between stakeholders



The big picture: Product value

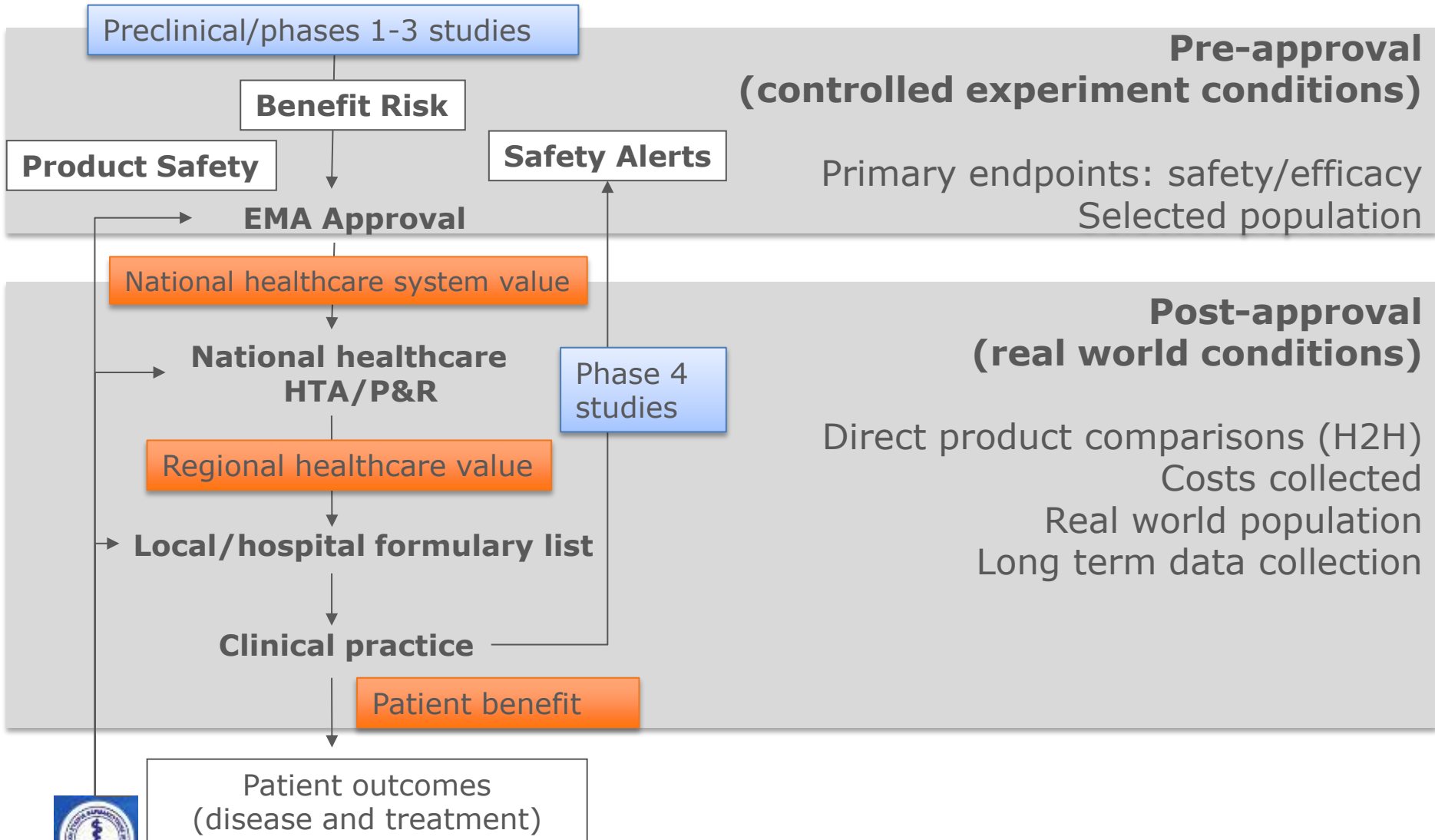


Challenges:

- Bridge gaps among stakeholders
- Align scientific methodology
- Share and link Real World Data (RWD)

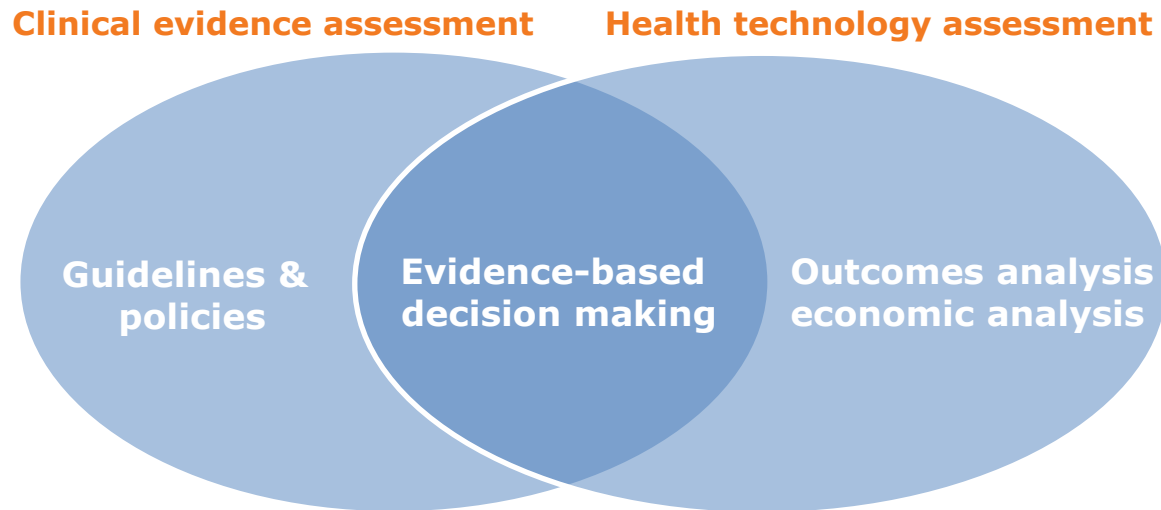


Value steps in the product life cycle



Evidence-based medicine & health technology assessment

Health technology assessment (HTA): “a multidisciplinary field of policy analysis, studying: medical, economic, social and ethical implications of development, diffusion and use of health technology”



Regulators:

Does the health technology work and is it safe?

Payors:

Is the health technology worth it?
Can it work in practice?



RWD in reimbursement decisions

What is real world data (RWD) in healthcare?

Data not collected in conventional randomized controlled trials (RCTs), providing an understanding of real life practice circumstances, from non-interventional studies

Outcomes (RWD in healthcare vs RCTs)

Endpoints	Comparators
Safety	Long term drug effect
Patient population	Economic implications

Research activity to gather RWD:

- Before product approval
- After product regulatory approval and marketing



HTA/P&R requirements in European countries

Need for RWD: health technology assessments, pricing & reimbursement

Country	Clinical trial	Economic analysis	Observational/epidemiology	Decision models	Post-marketing surveillance
Austria		✓	✓		
Denmark	✓	✓		✓	
France	✓	✓	✓		✓
Germany	✓	✓		✓	
Hungary	✓	✓	✓		
Italy	✓	✓			✓
Netherlands	✓	✓	✓	✓	✓
Portugal	✓	✓	✓	✓	
Spain	✓	✓	✓		
Sweden	✓	✓	✓	✓	✓
UK	✓	✓	✓	✓	



RWD input to projects that support product value



Pre-approval RWD generation

Pre-approval RWD collection includes:

- Epidemiological data
- Data on current patients' management
- Identification of unmet medical needs
- Determination of costs associated with a disease or treatment related-events, in terms of longer term outcomes, and in comparison with the current standard of care.
- Inputs for cost-effectiveness and budget impact models

Questions to answer:

- What is the actual incidence of treatment failure in real life?
- What is the burden of the disease to the patient or the wider society?



Post-approval RWD generation

RWD collection after regulatory approval allows:

- Effectiveness to be demonstrated against key competitors
- Generation of evidence on:
 - medication adherence
 - compliance parameters
 - long-term clinical events
 - differentiation in sub-populations
 - potential off-label use
 - evaluation of the changing treatment landscape.

Question to answer:

- What is the actual safety or effectiveness in real-world clinical settings vs observed drug efficacy?



RWD study designs and data collection

Study designs providing evidence for coverage and payment decisions:

Registries:

- Large patient population reflecting RW patients, management practices, and outcomes.



Claims databases/electronic medical records:

- Billing codes from health care providers (physicians, pharmacies, hospitals) submitted to payors (insurance companies, public healthcare system)

Practical or pragmatic clinical trials (PCTs) observational studies:

- Longitudinal care, drugs, devices, and diagnostic (biological or imaging) used.
- Developed to answer the questions faced by decision makers



RWD sources and types

Data source

Clinical

Economic

**Patient-reported
outcomes**

Data type

- Clinical outcomes (morbidity and mortality)
- Safety data
- Natural history of the disease
- Epidemiology
- Utility data for economic modelling
- Prescribing patterns
- Treatment pathways
- Health care resource use
- Health related quality of life
- Treatment preference/satisfaction



Supply of RWD (international examples)

National payor systems database size



National Health Service's *Clinical Practice Research Datalink* (20% UK population; anonymized patient records in primary care)



Nationella Kvalitetsregister (nationwide; 80 national registries covering diagnosis, treatment, outcome measures in various therapeutic areas)



BARMER GEK statutory health insurance (13% German population; records outpatient physician and pharmaceutical claims)

Private payors and integrated systems examples



Studies have linked inpatient and outpatient electronic medical records with claims among the following datasets:

- *Wellpoint's HealthCore* (34 million lives across 14 states)
- *Kaiser Permanente* health plan (9 million patients across 8 states)

Clinical IT systems providers examples



Allscripts and GE both offer access to de-identified clinical datasets on millions of patients via electronic health records systems (although limited longitudinally).

Clinical information systems in the US cover about 65% of hospitals and 35% of physicians' offices.



Science-based information in the real world setting

Scientifically valuable information that meets real world needs



Observational studies provide an opportunity for the science to yield commercial value at pre- and post-approval phases:

- Ethics approval when necessary
- Use of pre-defined statistical analysis plan
- Validation of instruments or questionnaires from experts (clinical, health economics)



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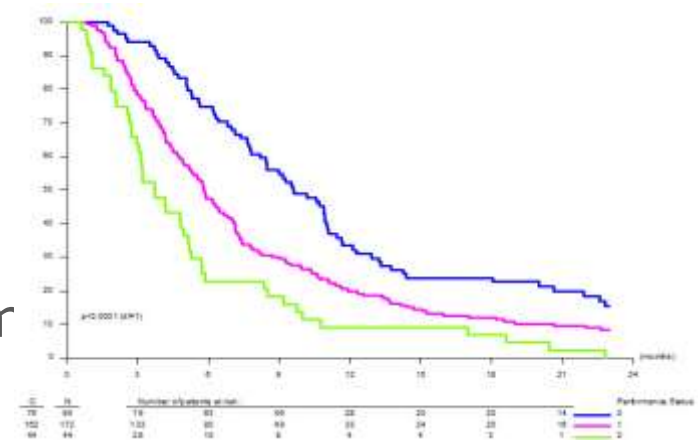
- Pre-approval
- Post-approval
- Niche segments



Examples in P&R (pre-approval)

1. Extrapolation of survival data based on RWD (cost-effectiveness models)

- Cost-effectiveness models can incorporate RWD (survival) (e.g., US SEER registry database, >60,000 patient records, for long term survival)



2. Costs of adverse events

- Primary research with clinicians: identifying the resource use for the management of SAEs (inpatient, outpatient)
- To be used for budget impact and cost-effectiveness analyses



Examples in P&R (pre-approval)

3. Treatment pattern surveys in oncology

Practicing clinicians in individual markets globally are surveyed in order to collect RWD on:

- current use of different treatments and standard of care (comparators)
- factors that influence treatment decisions (guidelines, biomarkers, line of treatment)
- treatment setting (hospitals, private office, residential)
- patient selection and definitions, including subpopulations
- adherence to treatment guidelines



Examples in P&R (pre-approval) Treatment patterns survey

Current management of advanced melanoma: a European perspective

Background

- Melanoma is a new but serious subtype of skin cancer that can infiltrate deep skin layers and commonly metastasize.
- Melanoma accounts for fewer than 5% of skin cancer cases but 60% of related deaths.^{1*}
- Melanoma affects all ages; however, 56% of affected patients are less than 55 years of age.^{2*} Thus melanoma can significantly affect work productivity and impact daily life.
- Median survival of patients with advanced (unresectable or metastatic) melanoma is less than 1 year.^{3,4*}
- Conventional chemotherapy does not provide any survival benefit for patients with advanced melanoma and, until recently, patients have been treated primarily with palliative chemotherapeutic agents such as dacarbazine and temozolomide.^{5*}
- Two new targeted agents, ipilimumab and vemurafenib, have been approved in the EU within the past 2 years for the treatment of advanced melanoma in adults; both have been shown to improve survival. During the period of the study they had the following indications:
 - Ipilimumab – treatment of advanced (unresectable or metastatic) melanoma in adults who have received prior therapy.
 - Vemurafenib – treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma.

Aims

- The aims of the study were to understand how advanced melanoma is currently being treated and to investigate clinicians' perceptions of the unmet need in the treatment of advanced melanoma.

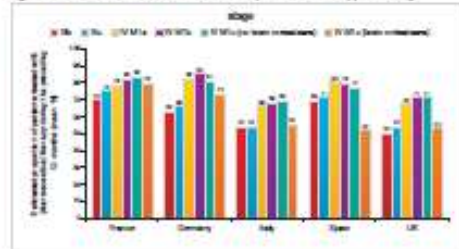
Methods

- A web-based survey of clinicians was designed to collect information about the treatment of advanced melanoma in France, Germany, Italy, Spain, and the UK. The survey covered the following themes:
 - treatment modalities used
 - drugs used for different stages of disease and/or for first, second, and third line of treatment
 - respondents' perceptions of the issues of greatest concern in the management of advanced melanoma.
- The survey was developed in collaboration with leading oncologists experienced in the treatment of advanced melanoma and was validated by one or two clinicians in each country. In total, 150 clinicians (30 in each country) were recruited (no more than three from the same hospital or center). The inclusion criteria were as follows:
 - dermatologist or oncologist prescribing pharmaceutical therapy and board-certified or accredited in their specialty
 - at least 2 years' experience in their current role
 - treated at least 10 patients with advanced melanoma (AJCC criteria) in the preceding 12 months.
- The survey was conducted between August and November 2012.

Results

- Most (66%) of the respondents were oncologists; 5% were dermatologists. Respondents had an average of 12.3 years' experience in their current (or a similar) role.
- Patient with melanoma represented about 25% of the total cancer case load of oncologists, and respondents had treated an average of 94 patients with advanced melanoma during the 12 months prior to completing the survey.
- Pharmaceutical therapy for advanced melanoma**
 - Pharmaceutical therapy was the predominant treatment for advanced melanoma (Figure 1).
 - The majority of patients with stage IV melanoma in France (81%), Germany (80%) and Spain (79%) were treated with pharmaceutical therapy, compared with 72%, 62%, and 70% of patients with stage III disease in these countries, respectively (Figure 1).
 - While about 90% of patients with stage IV disease in Italy and 70% of patients in the UK received pharmaceutical therapy, only 54% and 52% of patients with stage III disease, respectively, did so.
 - Approximately 51% of patients with advanced melanoma who received first-line treatment subsequently received a second line; few received third-line therapy (ranging from 0% in the UK to 17% in Germany and France).

Figure 1 Patients with advanced melanoma treated with pharmaceutical therapy at each stage



- Most respondents had used ipilimumab and vemurafenib for the treatment of advanced melanoma in the 12 months prior to completing the survey. The highest proportion of clinicians who had done so was in the UK (80% ipilimumab, 90% vemurafenib); the lowest proportion was in Spain (30% ipilimumab, 70% vemurafenib) (Table 1).

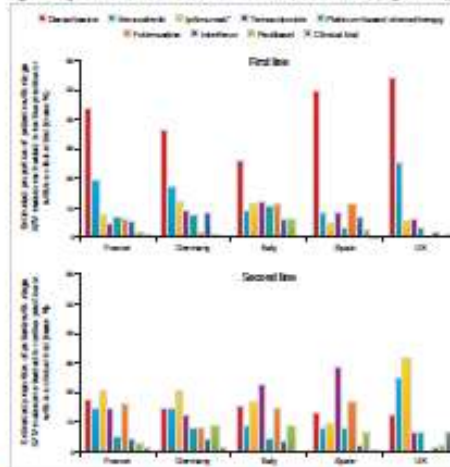
Table 1 Percentage of respondents (n = 150) by country with experience of using ipilimumab and vemurafenib

	France	Germany	Italy	Spain	UK
Vemurafenib	37	77	83	70	90
Ipilimumab	37	83	83	30	80

*Data for stage IV refers only to patients with brain metastases.

- Dacarbazine was the most commonly used drug in first-line treatment of patients with advanced melanoma. The mean estimated proportion of patients treated with dacarbazine in first line ranged from 30% in Italy to 54% in the UK (31% in Germany, 44% in France, 50% in Spain) (Figure 2).
- Ipilimumab was the most commonly used drug in second-line therapy in France (81%), Germany (90%), and the UK (80%), although a wide range of other drugs were also used (Figure 2).
- Vemurafenib is only indicated for tumors carrying the BRAF V600 mutation; the prevalence of patients with this type of melanoma is thought to be about 50%.^{6*} Vemurafenib was used for first-line therapy in an estimated 25% of patients in the UK, 16% in France, 16% in Germany, and 9% in Spain and Italy (Figure 2).

Figure 2 Drug use in the first-line and second-line treatment of advanced melanoma (stage III and IV)

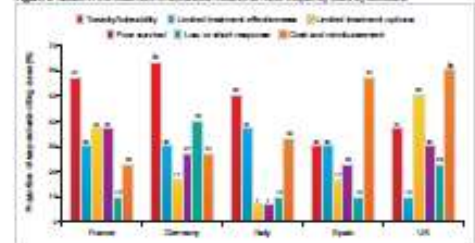


*Note: Clinical guidelines recommend only in a clinical trial for patients with unresectable disease, a number of trials involving ipilimumab in first line and for subsequent therapy are in progress. The reported use of ipilimumab in first-line therapy is likely to be within a clinical trial given that it is not currently licensed for first-line treatment.

Unmet need

- Overall, toxicity and tolerability of treatment was the most commonly mentioned issue from respondents (mean 47% across all countries) in the management of advanced melanoma, across all five countries: France (57%), Germany (60%), Italy (50%), Spain (50%), the UK (37%) (Figure 3).
- Limited treatment effectiveness was cited as an unmet need by 30% of respondents in France, Germany and Spain, and 37% in Italy; limited treatment options was the issue most frequently cited by clinicians in the UK (33%).
- A considerable proportion of clinicians from France, Germany, Spain, and the UK identified poor survival as a key concern in the treatment of advanced melanoma (France 37% respondents; UK 30%; Germany 27%; Spain 29%).

Figure 3 Issues in the treatment of advanced melanoma most frequently cited by clinicians



Conclusions

- The majority of clinicians surveyed had experience of using ipilimumab and vemurafenib in patients with advanced melanoma.
- Despite experience with ipilimumab and vemurafenib, clinicians highlighted a number of issues that remain in the treatment of advanced melanoma, suggesting that unmet need remains high. There is a continued need to increase the number of patients achieving complete response, prolong treatment-induced response, increase the number of patients surviving long term, and decrease severe treatment toxicities.

References

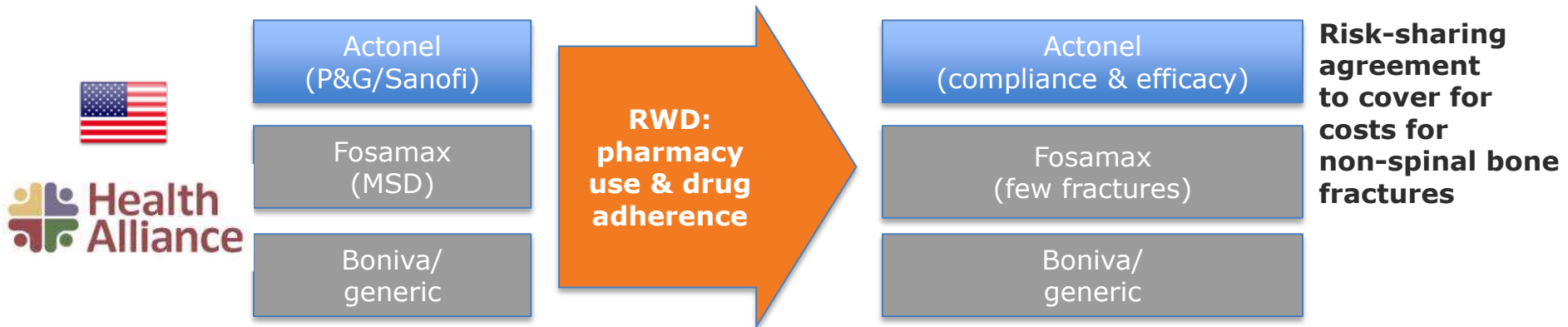
1. American Cancer Society. Cancer Facts & Figures 2011. 2. Kwon JS, et al. J Clin Oncol 2010; 28: 367-84. 3. Sauer A, et al. J Clin Oncol 2011; 29: 1164-70. 4. Paly J, et al. J Clin Oncol 2011; 29: 1164-70. 5. Sauer A, et al. J Clin Oncol 2011; 29: 1164-70. 6. Flaherty KT, et al. N Engl J Med 2012; 366: 110-9.

This poster was presented at an international conference in 2013.



Examples in P&R (post-approval/market)

1. Maintain preferred formulary status (osteoporosis):



2. Challenge and defend efficacy of product class (insulin analogues)

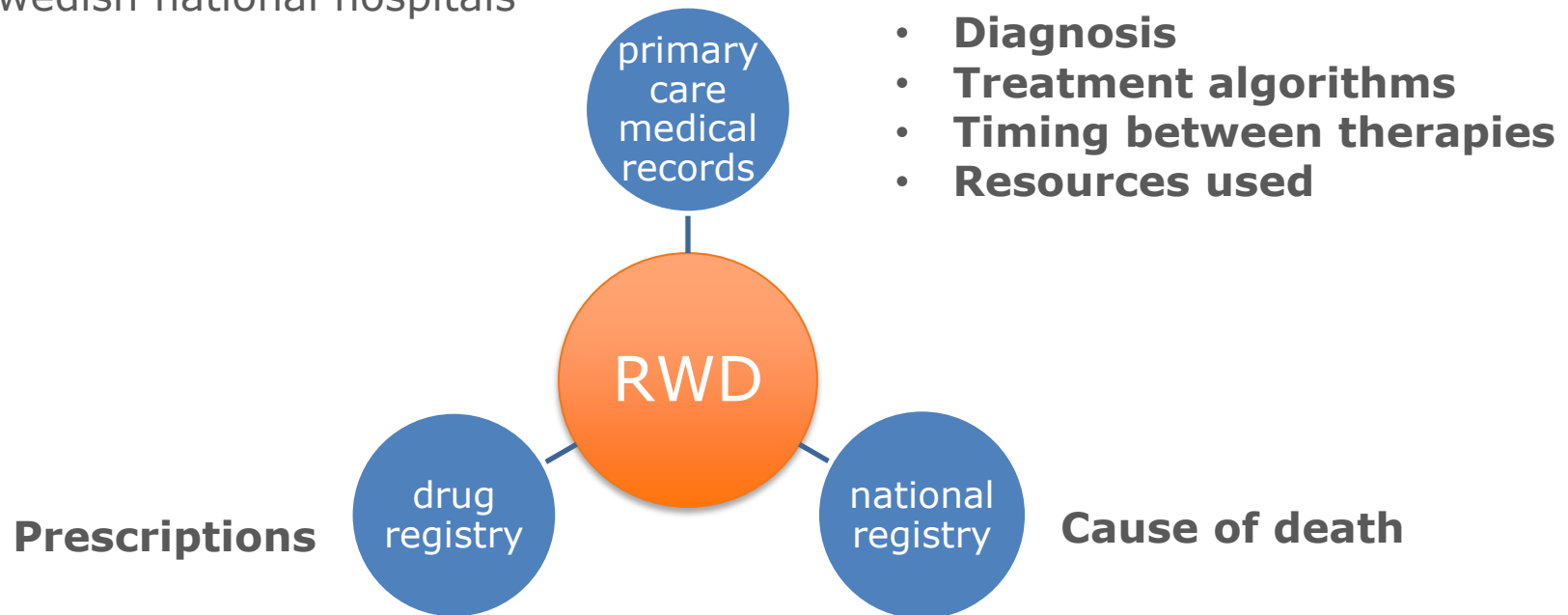
In 2010 long-acting insulin analogues were excluded from reimbursement list



Case studies in P&R (post-approval/market)

AstraZeneca PATHOS retrospective observational registry study in moderate to severe COPD:

 Swedish national hospitals



Results: Budesonide/formoterol more effective than fluticasone/salmeterol in preventing COPD exacerbations. Use of former appears to reduce hospitalization, emergency visits, and use of oral steroids and antibiotics.



Niche market segments

Orphan drugs: limited clinical data lead to reliance on RWD



Example: ZonMW (the Netherlands) funds hospital care based on the conduct of outcomes research studies, and re-evaluation after 4 years by CVZ



Companion diagnostics: different reimbursement models

(e.g., Payment for Tx/Dx provided there is RWE on clinical benefit)



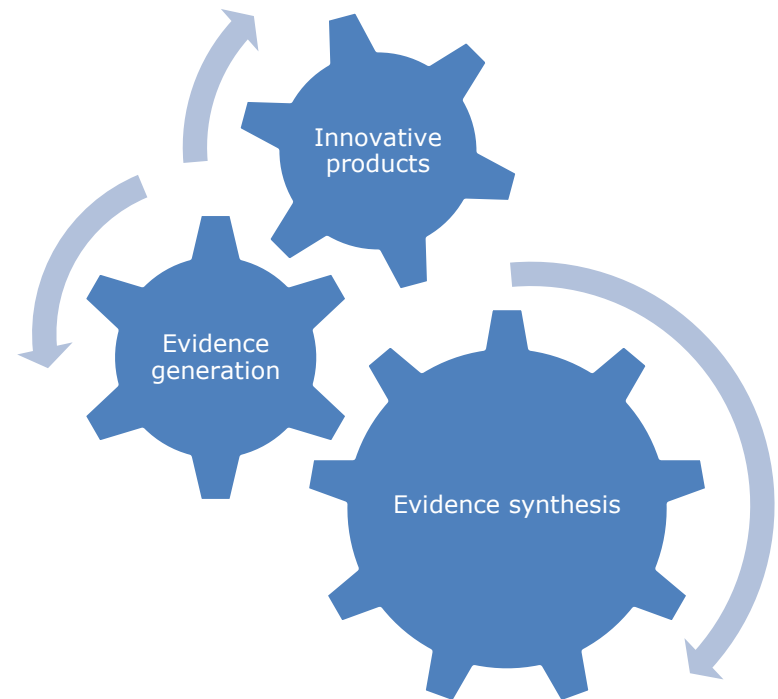
Example: PBAC (Australia) has developed a clear set of guidelines to assess Dx:

- prevalence of a true positive biomarker in the population likely to receive the test
- linked evidence available of the test's impact on patient health outcomes



Summary of presentation

- RWD are widely used for pricing and reimbursement decisions
- Clinical, economic and PRO RWD are essential for decision-making
- Pre- and post-approval RWD oriented projects support value claims throughout the product lifecycle



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