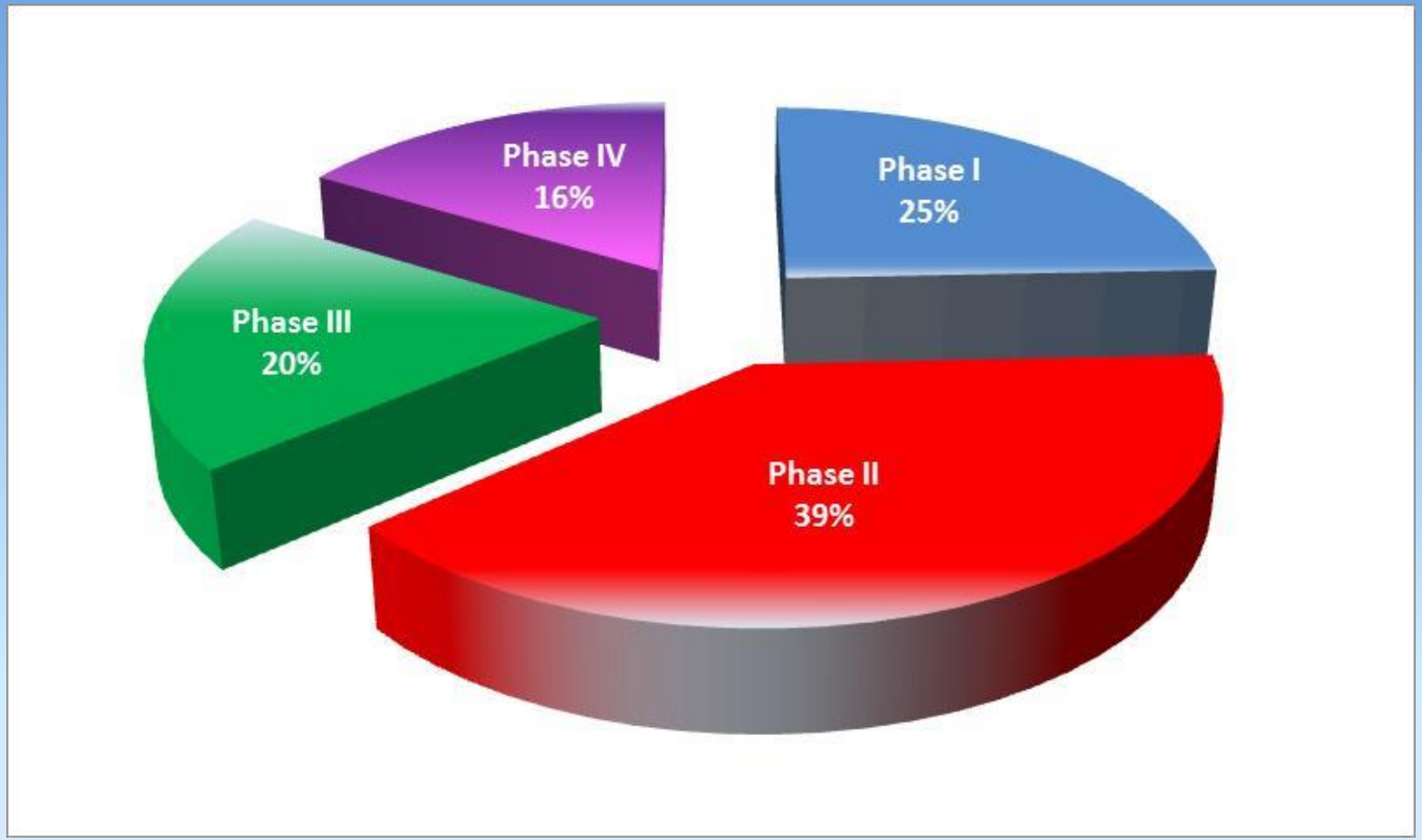
Development of Horizon Scanning activities and implications for Africa

Third Training Workshop and Symposium MURIA Group
University of Namibia, Windhoek , 26 – 28 June 2017

Roberta Joppi
Italian Horizon Scanning Project – Local Health Authority of Verona, Italy
Chair of EuroScan International Network

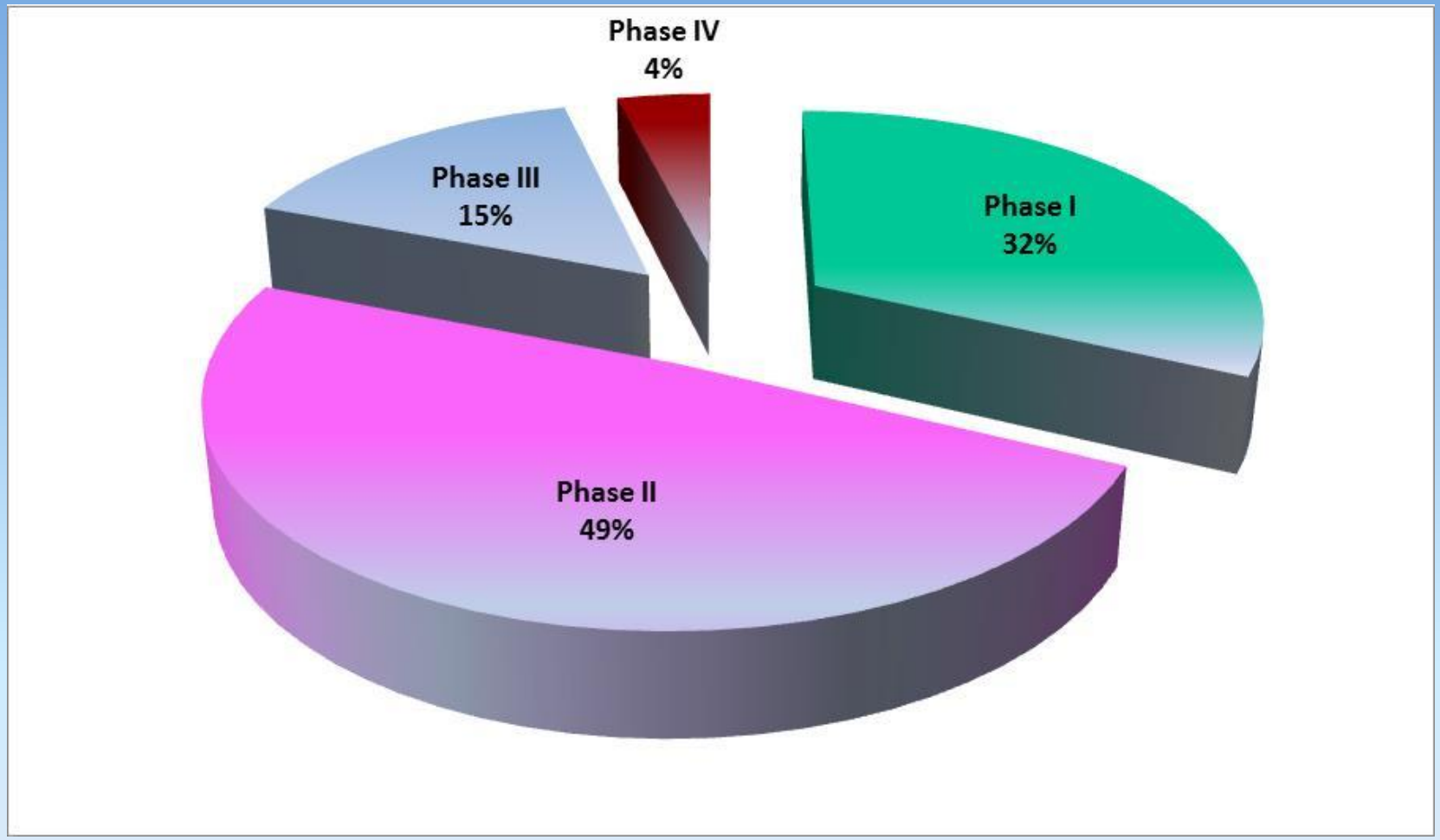
24,999 RCTs are now recruiting in the World



https://clinicaltrials.gov/ accessed 09/06/2017

Onco RCTs recruiting in the World: 10,372

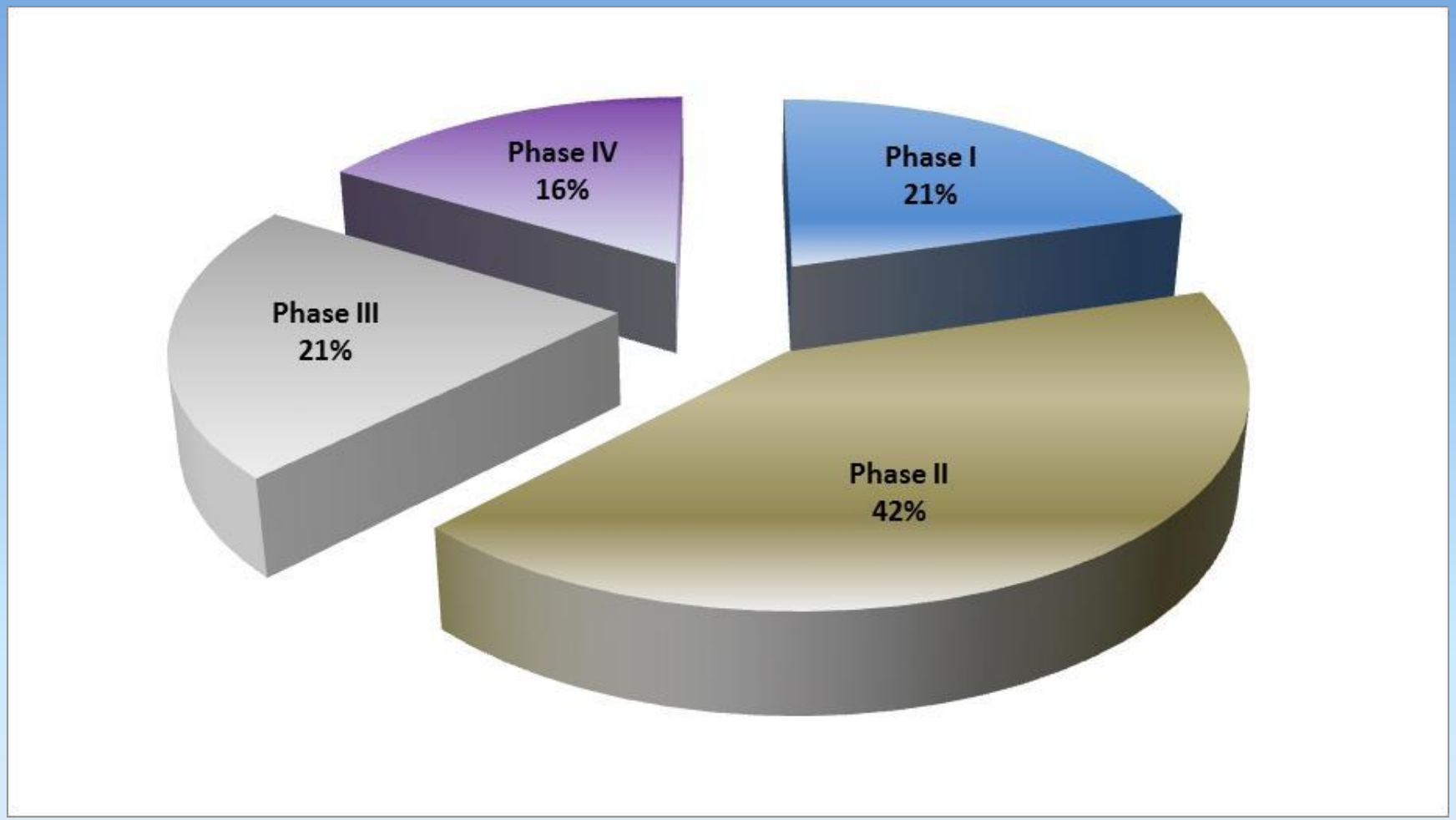
(41% of all ongoing RCTs)



https://clinicaltrials.gov/ accessed 09/06/2017

RCTs on Antibiotics recruiting in the World: 1,912

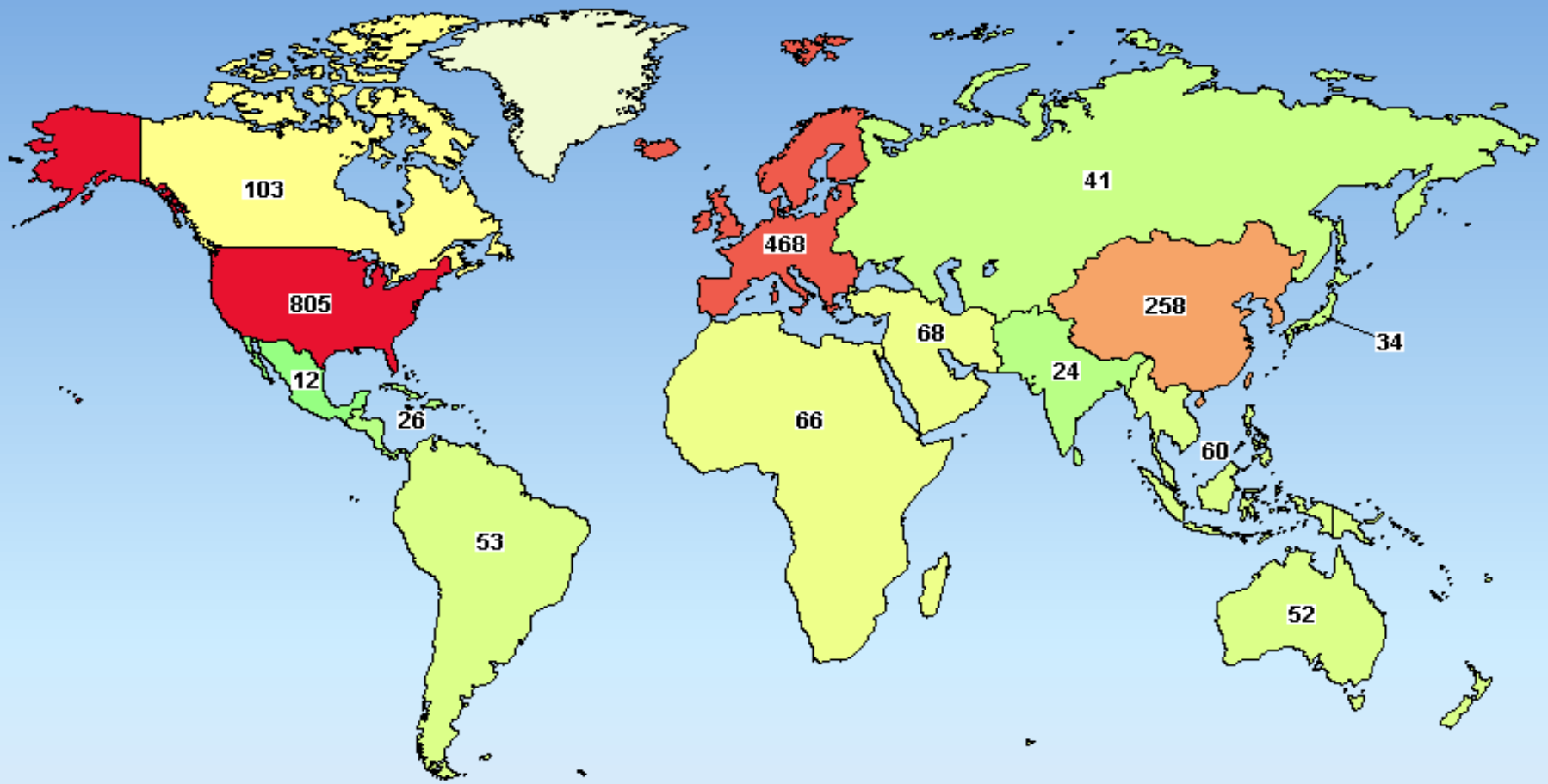
(6.8% of all ongoing RCTs)



https://clinicaltrials.gov/ accessed 09/06/2017

EuroScan
International Network

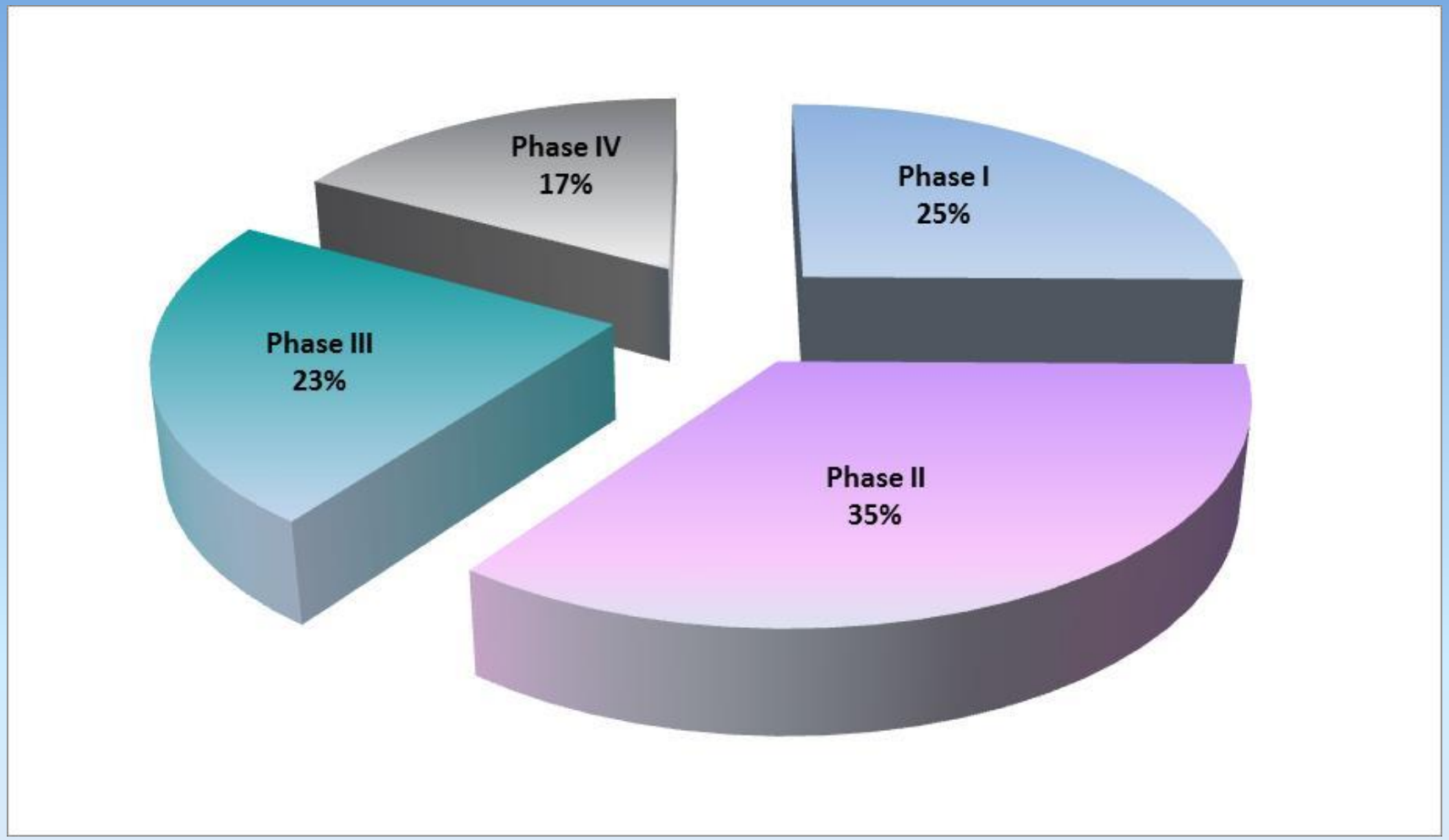
Distribution of recruiting RCTs on Antibiotics



https://clinicaltrials.gov/ accessed 09/06/2017

RCTs on ant-HIV drugs recruiting in the World: 405

(1.6% of all ongoing RCTs)



https://clinicaltrials.gov/ accessed 09/06/2017

EuroScan
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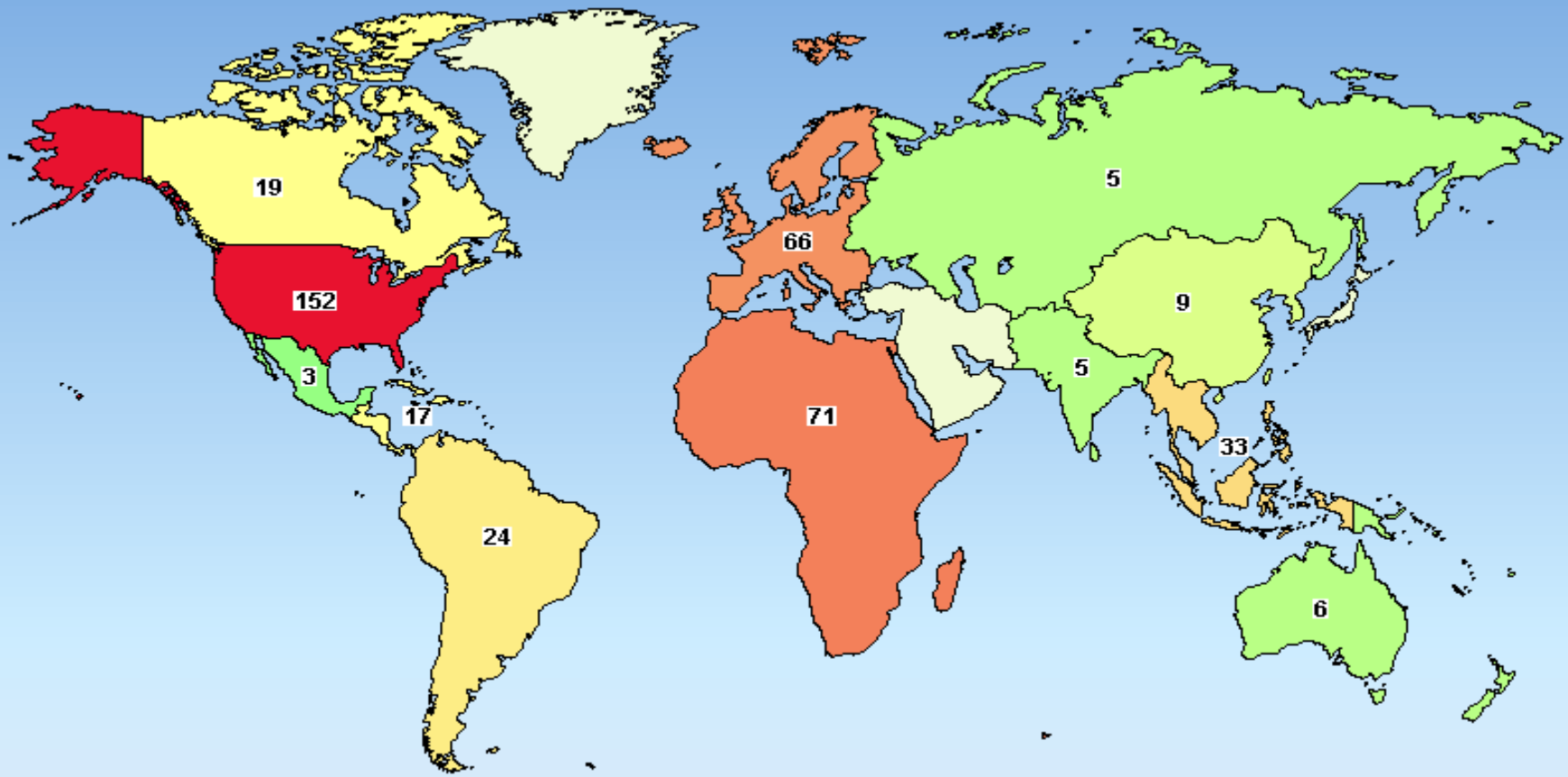
Distribution of recruiting RCTs on ant-HIV drugs



https://clinicaltrials.gov/ accessed 09/06/2017

RCTs on Neglected Diseases now recruiting in the World: 70

(0.3% of all ongoing RCTs)

Neglected Diseases (WHO)	Number of Studies (Open/Interventional/Phase 1,2,3,4)	Location
Dengue	17	Central America (2); North America (6); South America (2)
Leishmaniasis	11	South America (6); Africa (2); Middle East (1); South Asia (2)
Lymphatic filariasis	9	South America (3); Africa (8); South Asia (3); South East Asia (4); Europe (1)
Rabies	7	North America (3); South Asia (1); South East Asia (3)
Chagas Disease	5	South America
Schistosomiasis	5	Africa (3); South America (1); Europe (1)
Chikungunya	3	North America (1); Central America (1); Europe (1)
Onchocerciasis	3	Africa (2); Europe (1)
Soil-transmitted helminthiasis	3	Africa (3); South Asia (1)
African Trypanosomiasis	2	Africa (2)
Cysticercosis	2	South America (2)
Trachoma	2	Africa (2)
Leprosy	1	East Asia
Bruli Ulcer; Dracunculiasis; Echinococcosis; Yaws; Fasciliasis	0	/

https://clinicaltrials.gov/ accessed 09/06/2017

What is an Early Awareness and Alert (EAA) System?

EAA systems are also known as Early Warning Systems or Horizon Scanning Systems

Aim to:

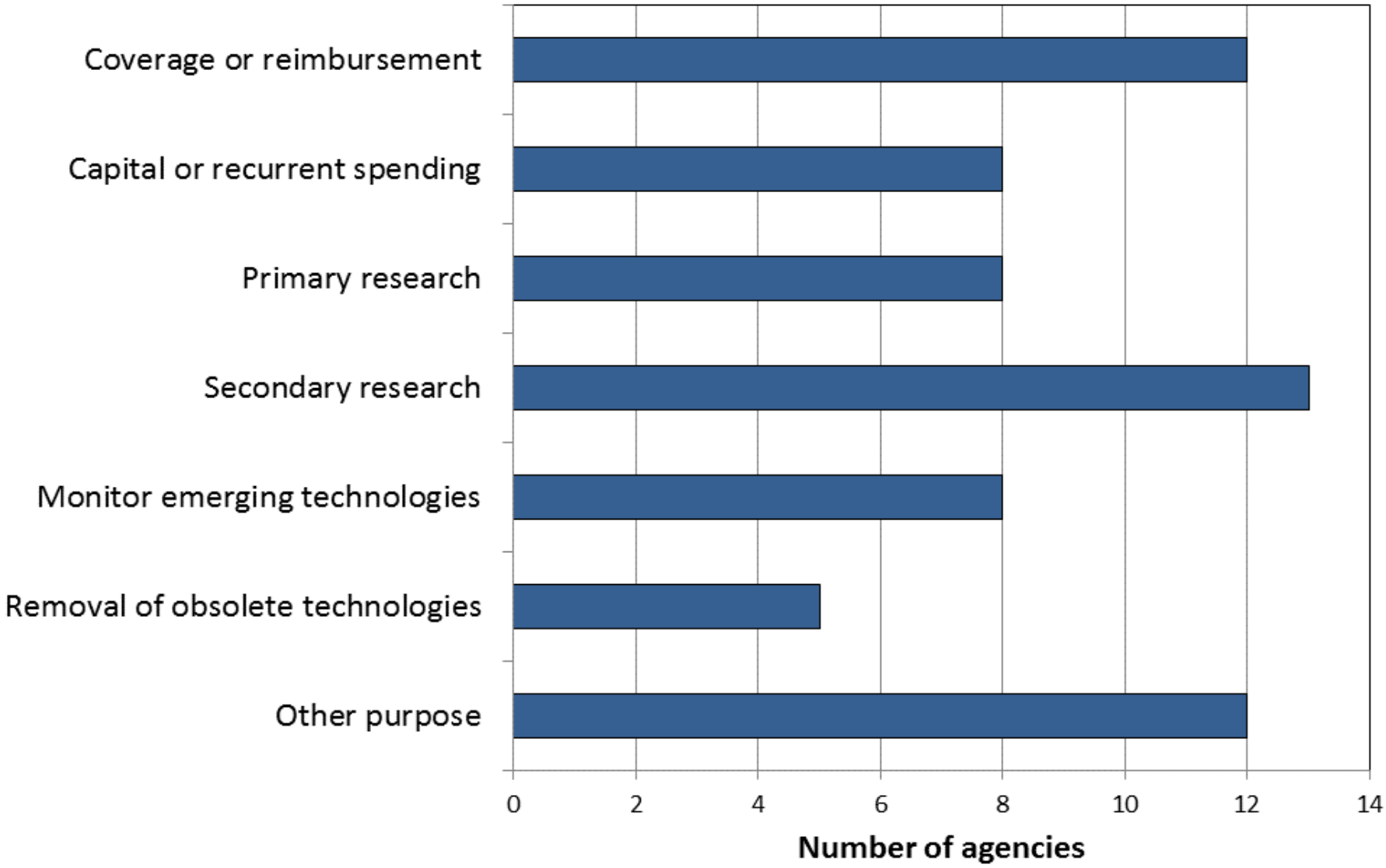
- identify, filter and prioritise new and emerging health technologies;
- assess or predict the impact of emerging technologies on health, costs, society and the healthcare system; and
- inform decision makers, research planners, health care professionals, patients and patient organisations.

Benefits of implementing an EAA System

EAA systems:

- ✓ ensure that there is a systematic approach to identifying important new and emerging health technologies;
- ✓ ensure that technologies are considered for evaluation at the right time, before widespread diffusion, thus protecting patients from ineffective and potentially unsafe health technologies and supporting the uptake of innovative, cost effective health technologies;
- ✓ alert policy makers and health service organisations to health technologies that could change current options or decisions (i.e. require revision of current guidelines, and/or further planning or research);
- ✓ ensure processes are put in place to support and monitor clinical development;
- ✓ raise awareness of 'lower-profile' or obsolete technologies.

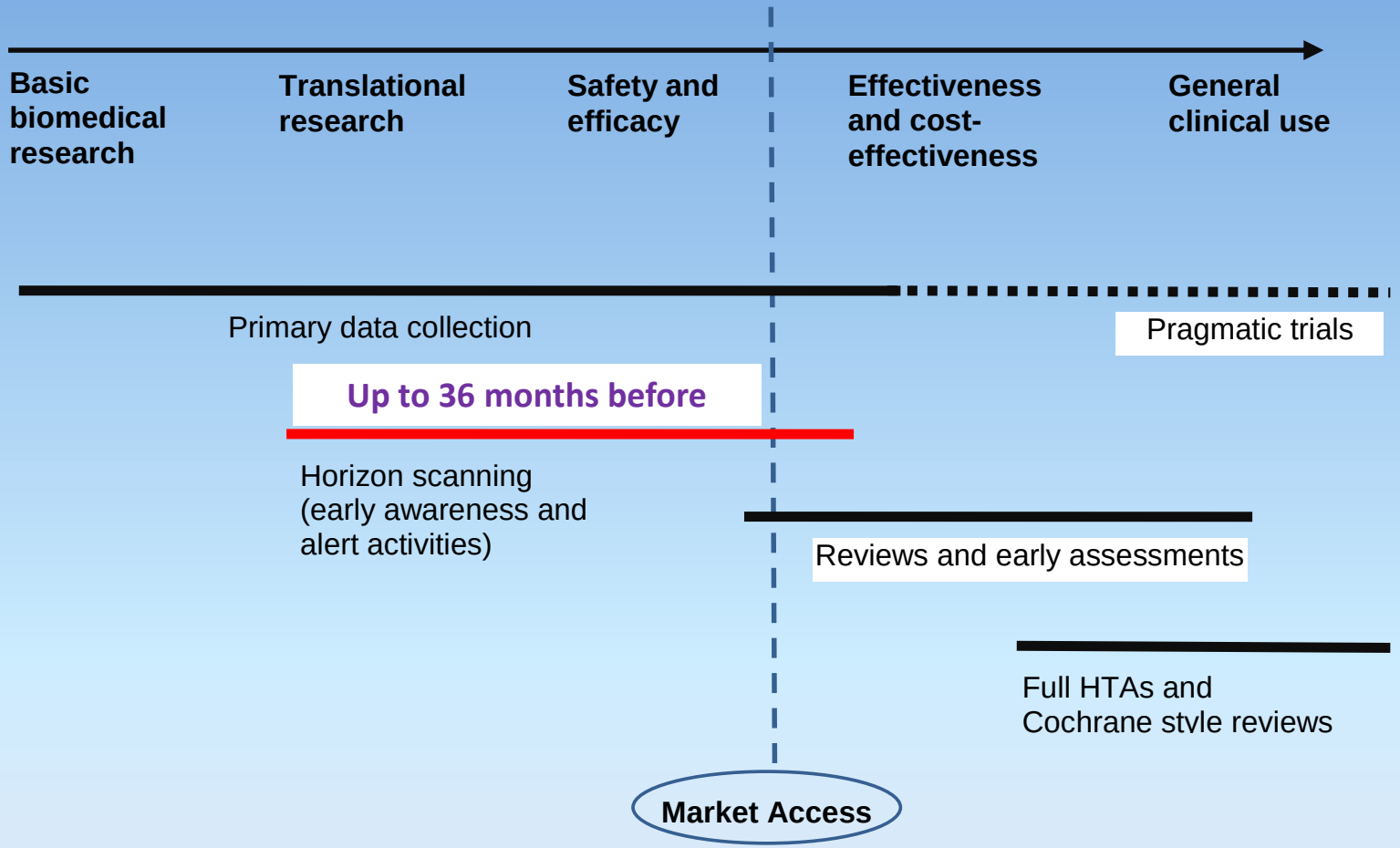
EuroScan: purpose of EAA system

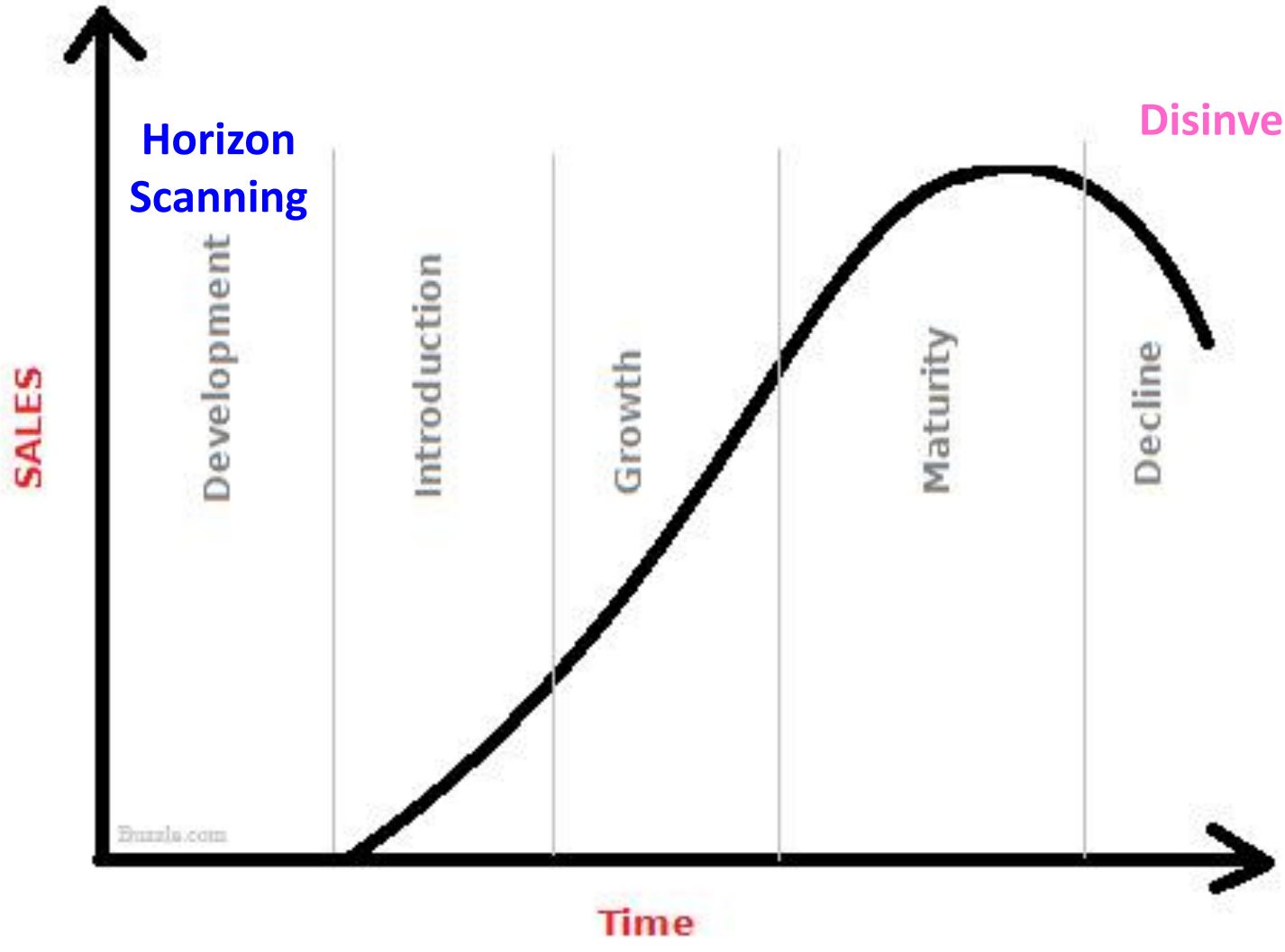


Packer C. et al. EuroScan International Network Member Agencies: their structure, processes and outputs. Int J Technol Assess Health Care 2015; 31(1-2): 78–85.

Where do EAA systems fit in?

EAA activities are part of a continuum of HTA activities





STAGES OF PRODUCT LIFE CYCLE

EuroScan
International Network

The international information network on new and emerging health technologies

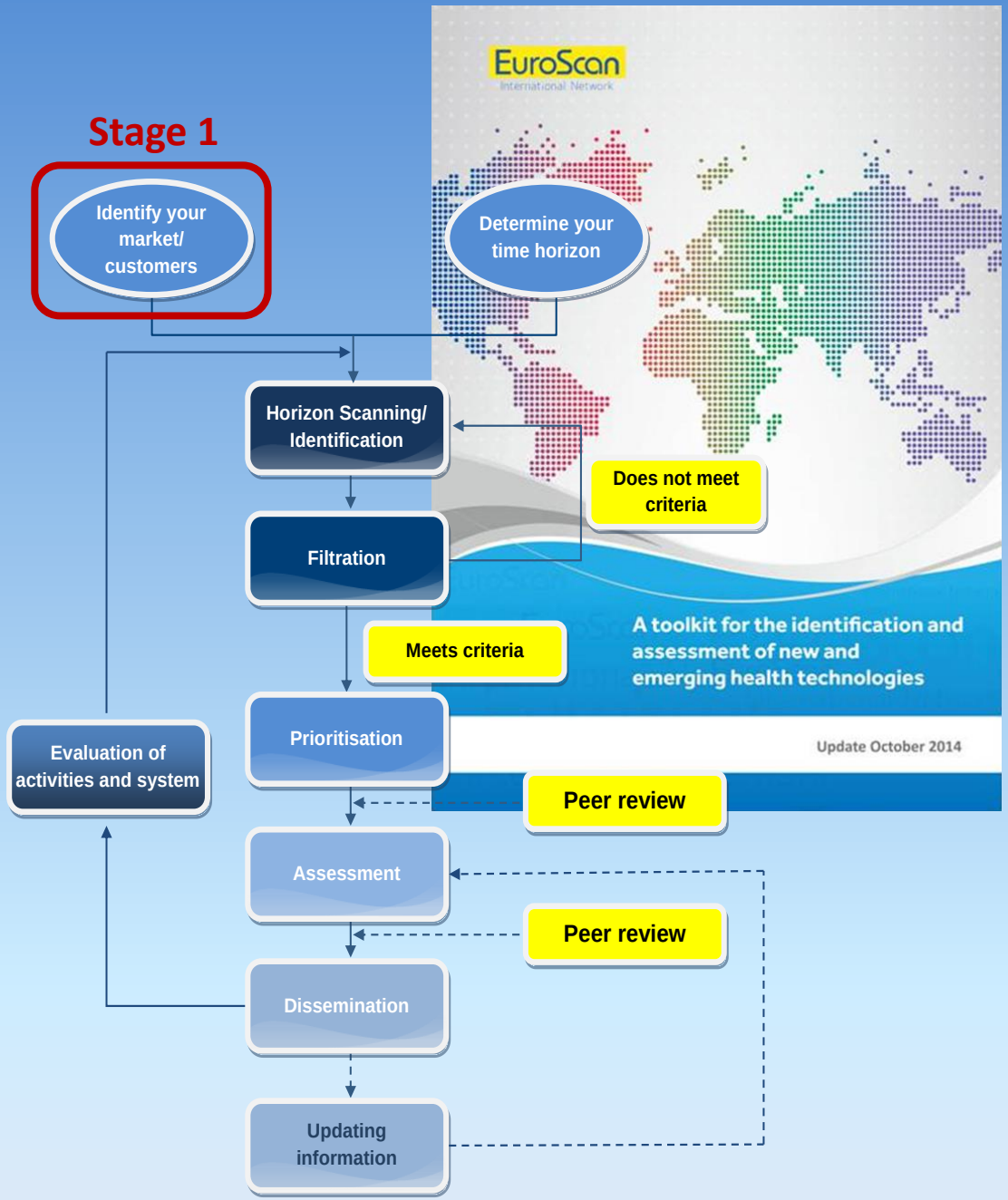
"A collaborative network of member agencies for the exchange of information on important emerging, new and obsolete technologies and the principal global forum for the sharing and development of methods for the early identification and assessment "

17 members representing Agencies in 14 different Countries

Members in four continents: Asia, Oceania, Europe and America

EuroScan Methods Toolkit

- Collaborative document covering all members approaches to EAA activities (identify, select, evaluate important emerging health technologies);
- Provides valuable information to those interested in establishing, or improving an existing EAA system;
- Already available in English and Russian; Spanish, French and Portuguese versions soon available.



First step…

The first step in developing an EAA system is to clearly define who the **target audience** will be and what the **objective** is for the activity.

Questions which should be addressed are:

1. **Who do you intend to inform** (e.g. policy makers, commissioners, purchasers, healthcare professionals/providers, reimbursement agencies, HTA agencies, commissioners of research, patients and patient organizations ; local/regional/national level)**?**
2. **What does your customer expect from you** (e.g. comprehensiveness, number of outputs, depth, frequency and timing, skills and prior knowledge of customers, confidential reporting or open documents) **?**
3. **What type of output and information is needed** (e.g. Brief overview (1-2 pages) or in-depth early assessment of efficacy, formal report or newsletter, paper or electronic)**?**
4. **What is the scope of your EAA system** (e.g. technology type (pharmaceuticals, devices, diagnostics, etc.), hospital, primary care or community setting, patient groups)**?**

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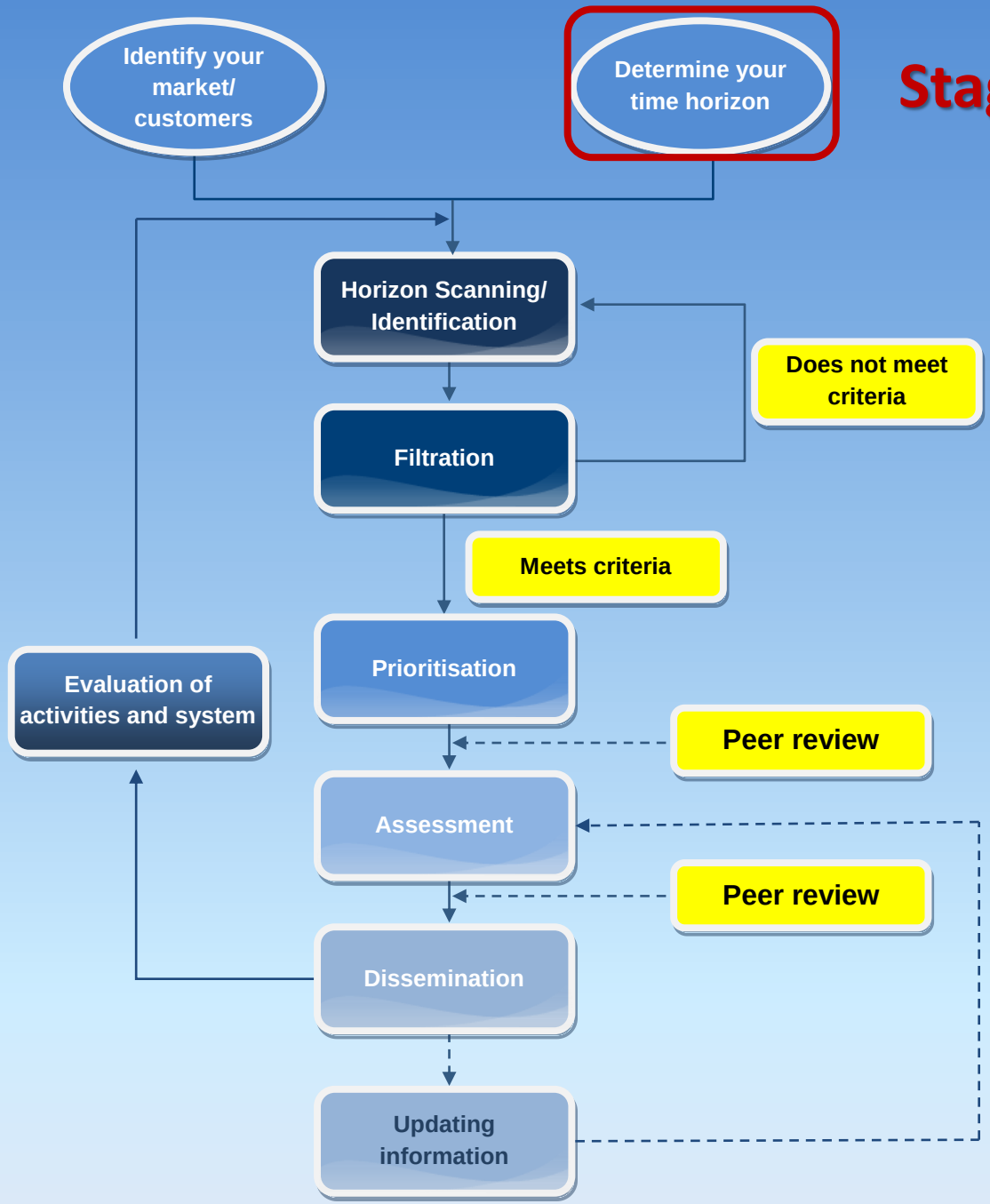
Stage 2

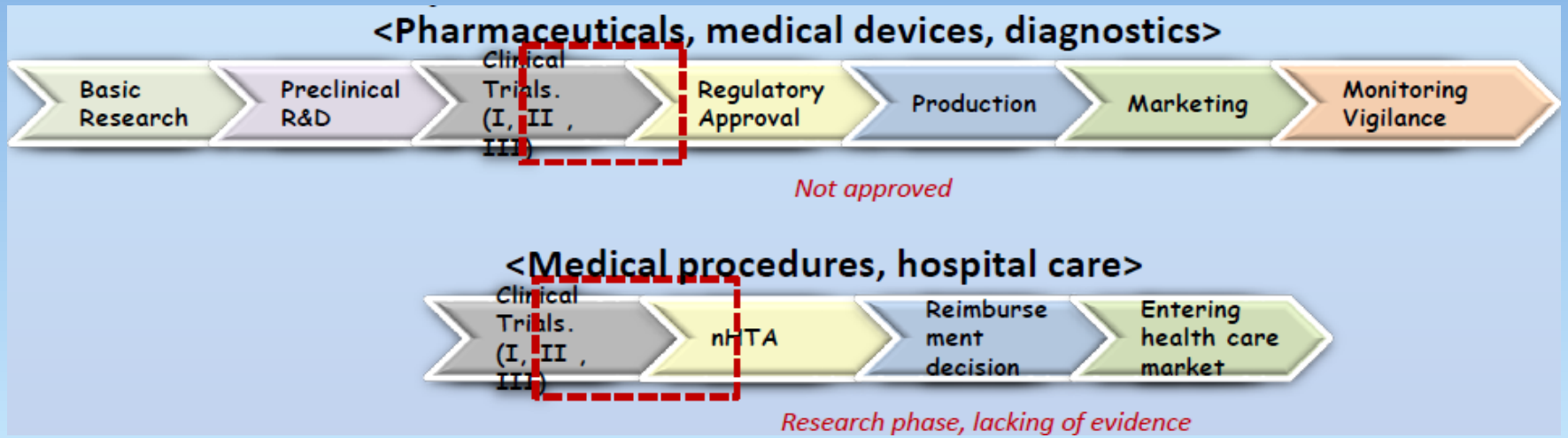


Typical time horizons

- Many EAA system use a 0 to 3 year time horizon (**near horizon**)
- Some look ahead up to 5 years (**distant horizon**) – particularly for larger trends (e.g., 3D printing, precision medicine….)
- Most technologies of interest will likely be on the near horizon (i.e., within a year of being marketed, or newly licensed & in early stage of diffusion)

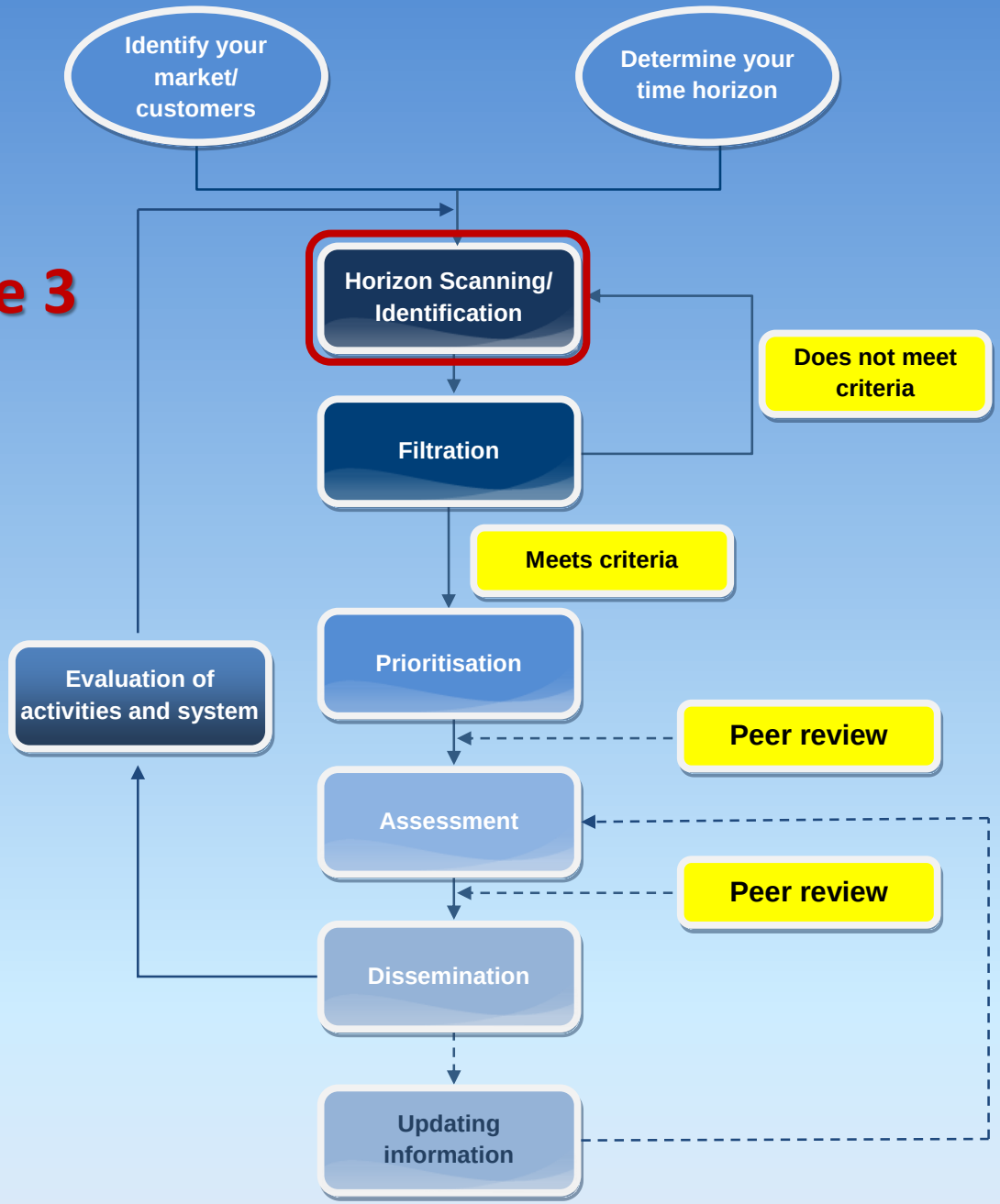
Technology lifecycle

- Information may be needed at various points over the technology's lifecycle, from early alerts and awareness to obsolescence (for possible disinvestment)
- Many technologies that appear promising never make it to the market
- The further from marketing or widespread use the less "good" evidence may be available



1-5 years before the Technology enters the Korean Health Care System

Stage 3

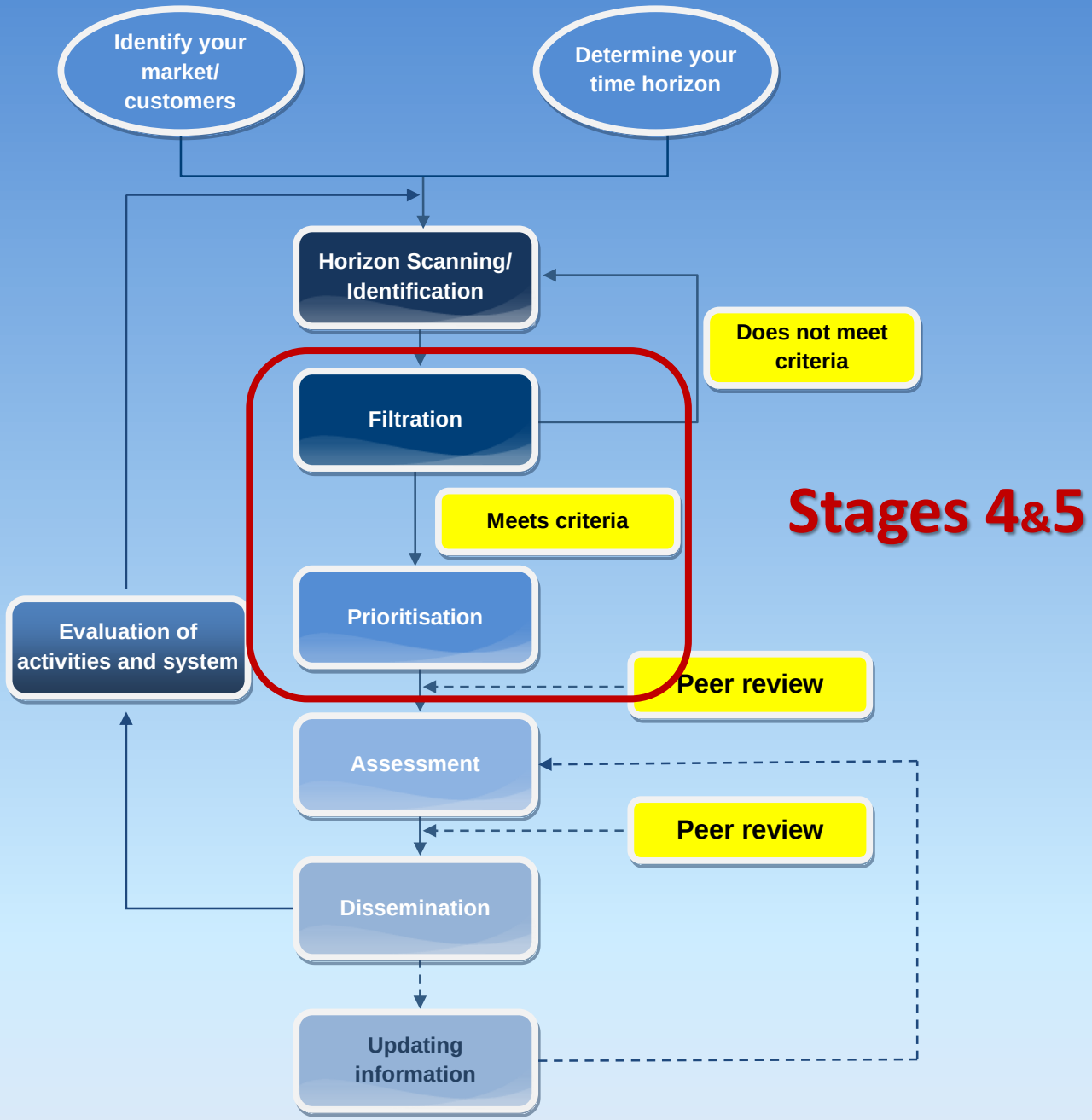

Identify your market/ customers
Determine your time horizon
Horizon Scanning/ Identification
Does not meet criteria
Filtration
Meets criteria
Prioritisation
Evaluation of activities and system
Peer review
Assessment
Peer review
Dissemination
Updating information

Types of identifications sources

Primary sources: information is obtained directly from sources closest to the technology (e.g. pipeline information from commercial developers, Clinical Trial Registers, Patent Applications)

Secondary sources: information is obtained from sources that have used primary sources but may have edited or filtered the information (e.g. Commercial & Medical Media, Scientific Sources (Conference proceedings, Scientific journals), Regulatory authorities, Experts)

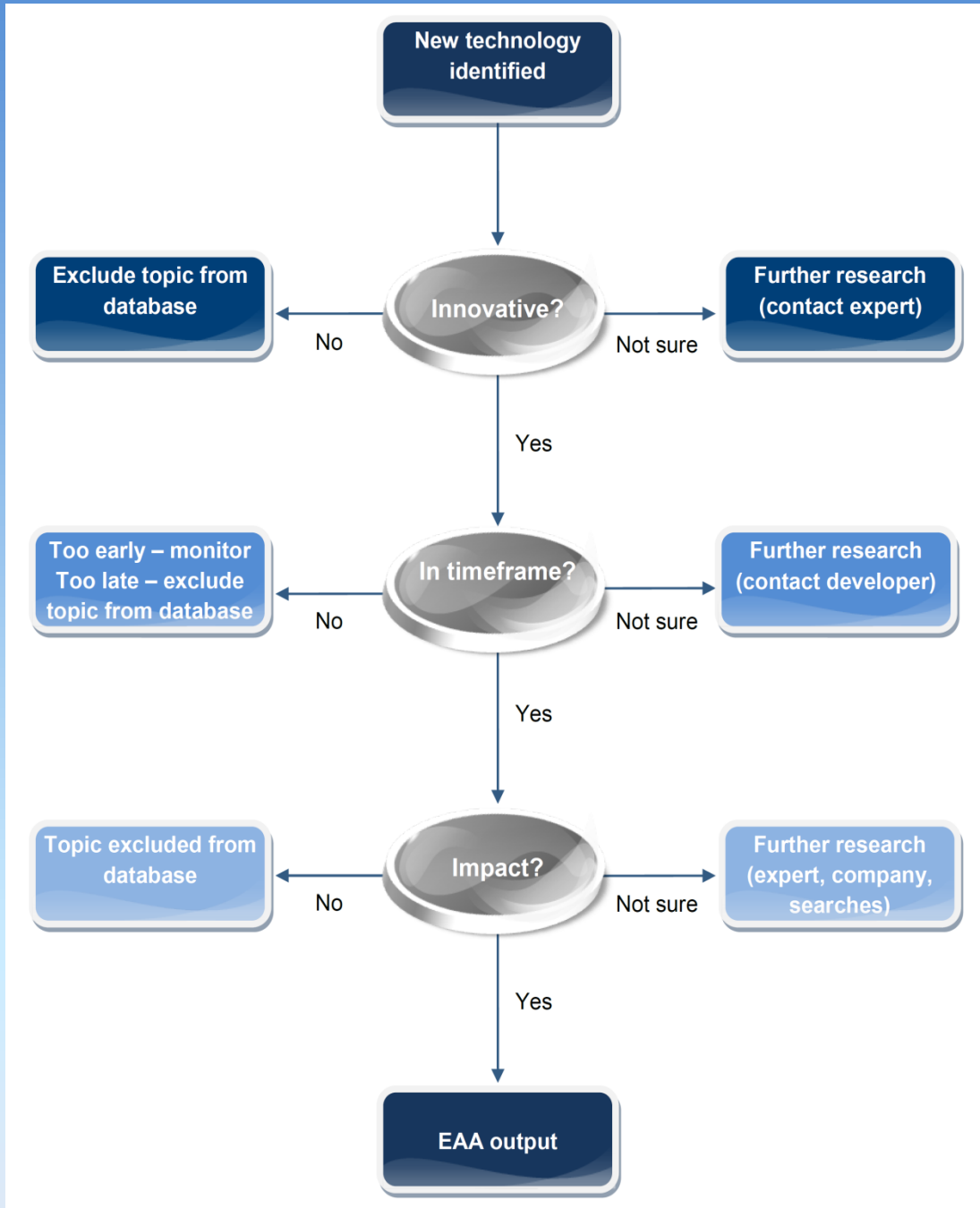
Tertiary sources: information is obtained from sources that have prioritized the information themselves and perhaps carried out an assessment (e.g. EuroScan, Other Early Awareness and Alert Systems)


Identify your market/ customers
Determine your time horizon
Horizon Scanning/ Identification
Does not meet criteria
Filtration
Meets criteria
Stages 4&5
Prioritisation
Evaluation of activities and system
Peer review
Assessment
Peer review
Dissemination
Updating information

Filtration

- ✓ Technologies found at the identification stage are considered;
- ✓ By applying **pre-set criteria**, technologies that are relevant to your EAA system and stakeholder are selected.

Filtration facilitates the best use of available resources.



Examples of Filtration Processes used by different EuroScan Agencies

Assessors

Three internal researchers and three regulatory experts

Criteria

1	Appropriateness (Suitability)	Manageable & acceptable? (Ex. Maggot, Meditation therapy)
2	Innovativeness	New and innovative? Or modified existing technology? Treatment efficacy is significantly improved? Having high accuracy and precision? *(diagnostic test)* Effective on manufacturing step or cost reduction?
3	Possibility of market entry	Entering into Korean health care system within 1-5 years? Clinical trial is expected to be terminated in 1-2 years, or has been terminated? Approved by Ministry of Food and Drug Safety (MFDS)?

Proposals are filtered according to the following criteria:

- Not being previously evaluated (by Osteba or other Spanish Agencies)
- Included or could be included in the benefit package;
- Under the remit of Osteba;
- Regulatory processes finished or nearly finished:
  - EMA or Spanish Agency for Drug and Medical Devices
  - CE mark for Medical Devices
  - Other required regulations
- Sufficient arguments that the proposal requires evaluation

Prioritisation

✓ Technologies selected from the filtration process are prioritized according to the system's capacity for assessment or evaluation of the technologies and customer requirements;

✓ Prioritization should be based on a pre-defined set of prioritization criteria based on stakeholder and customer requirements is recommended (soring tools can be used)

Due to a potential conflict of interest, prioritization does not usually involve industry or commercial developers or clinicians and researchers who work closely with a technology.

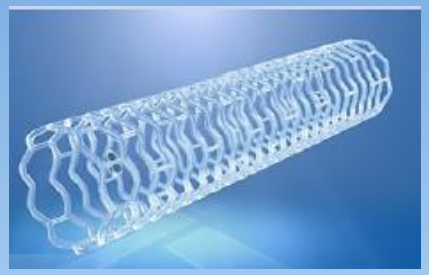
Examples of Prioritization by different EuroScan Agencies

HEALTH PACT

- **Once identified technologies prioritised according to pre-defined criteria**

- Clinical need
- Rate and pattern of diffusion
- Estimated clinical impact
- Estimated cost impact
- Efficacy and safety issues
- Ethical issues
- Cultural or religious issues
- Other

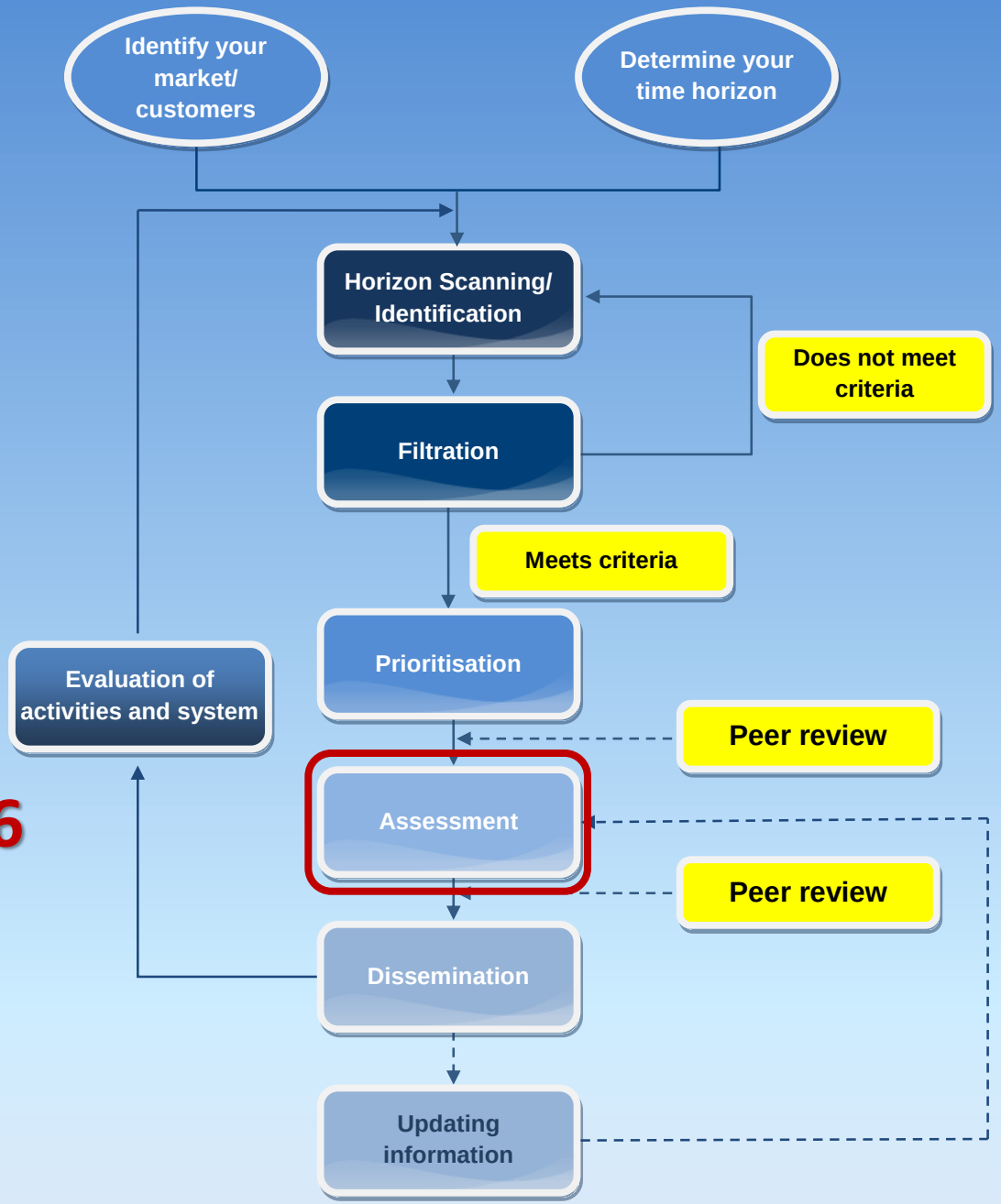
The technology has not been assessed and is rapidly diffusing throughout the Australian Health System



- Bioresorbable stents
- Rapidly diffusing similar to drug-eluting stents
- Evidence-base poor with no demonstration of superiority
- Financial impact on all jurisdictions

The Technology is a potential opportunity for disinvestment

- Stenting vs. Medical Therapy for renal-artery stenosis
- Thought to prevent the development of adverse CV and renal events, BUT introduced into clinical practice with no evidence to support its use
- Appropriate for a small subset of patients or as a last resort
- Clinical practice guidelines need to be updated to reflect this change in clinical practice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Does not meet criteria
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Meets criteria
Prioritisation
Evaluation of activities and system
Peer review
Assessment
Peer review
Dissemination
Updating information

Stage 6

Assessment

Different types of assessments

- Rapid: brief overview (1-2 page), conducted in response to a specific question;
- Brief: overview (4-6- pages), includes: background on the technology, clinical burden of the disease, safety/efficacy evidence, current comparator(s), costs/social/ethical/legal concerns;
- In-Depth: focused assessment using a structured strategy (≥40 pages)

Methods for assessment

- Developing an assessment template that remains unchanged for all assessments (e.g. technology related info; pts and setting related info; evidence and policy; impact predictions
- Developing a search strategy, whose comprehensiveness will depend on the type of assessment
- If possible (and applicable) it is recommended to specify criteria for selecting studies, quality assessment, and grading of evidence

Involvement of

- Companies and developers to obtain info such development status, regulatory or marketing plans, unpublished/ongoing studies, and pricing information about a technology
- Experts: to provide information and advice during the assessment process. It is recommended to involve more than one expert to ensure that a range of views are considered

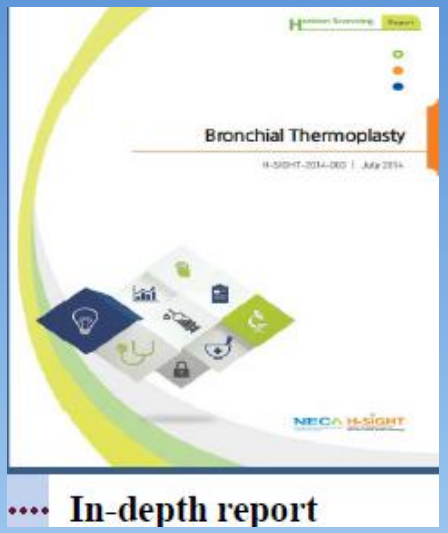
Scientific uncertainties

It is recomended to include a description of what the uncertainty encompasses, and what kind of research is needed to fill the gap in the future

Examples of Assessment Reports by different EuroScan Agencies

Reports

In-depth Report (electronic, Korean English, ≥ 20 pages



Brief Report (electronic, Korean, English, 3-4- pages

Newsletter (electronic, Korean, quarterly, 2-3- contents/newsletter)

IHSP Outputs

-36 MONTHS REPORT

Produced annually

- general information
  - *Drug/brand name/ active substance*
  - *Company*
  - *ATC Group*
- licensee
- stage of development
- possible submission date of the MAA
- main proposed indication(s)
- ongoing studies

-18 MONTHS REPORT

Produced every 6 months

- general information
  - *Drug/brand name /active substance*
  - *Company*
  - *ATC Group*
  - *Route of administration*
- possible submission date of the MAA
- proposed indication(s)
- summary of the available data on clinical efficacy and safety
- overview of all ongoing trials and completed studies not published
- possible price and economic impact (if available)
- alternative(s) already on the market
- possible competitors in development

NPIR

(-12 months to M.A.)

"Drug Name"
"Drug Indication"

- general information
  - *Active substance*
  - *Brand name*
  - *Company*
  - *ATC Group*
  - *Dosage*
  - *Route of administration*
  - *Development state*
  - .....
- clinical need and burden of disease
- summary of efficacy/safety data from available clinical trials
- clinical critical assessment
- social / economic impact
- ongoing trial(s) for the same or other indication(s)

EuroScan International Network

Horizon Scanning Research & Intelligence Centre

NHS National Institute for Health Research

July 2016

Horizon Scanning Research & Intelligence Centre

Nilvadipine for mild to moderate Alzheimer's disease – first or second line

LAY SUMMARY

Alzheimer's disease is a disease that affects the brain, causing dementia. It is a progressive disease, which means that gradually more of the brain is damaged, so that over time more symptoms

Technology ALERT

May 2016

Horizon Scanning Research & Intelligence Centre

The Vivistim® System for upper-limb deficit after a stroke

TIMEFRAME: Estimated earliest commercial availability in the UK

Currently unclear | Now | 6 months | 1 year | 18 months | 2 years | Over 2 years

Click here for Lay Summary

TECHNOLOGY

The Vivistim® System is an implantable device developed by MicroTransponder Inc. for the rehabilitation of patients with upper-limb deficit after a stroke.

© MicroTransponder Inc.

The Vivistim® System consists of an implanted pulse generator (IPG), stimulator and lead and an external wireless transmitter, computer, remote control and software. The stimulator is placed on the left vagus nerve in the left carotid sheath. The lead is then tunnelled subcutaneously to a pocket created in the left pectoral region where it is attached to the implantable Vivistim® pulse generator. The clinician initially programs the IPG using the computer and software and initiates vagus nerve stimulation (VNS).

Technology ALERT

July 2016

Horizon Scanning Research & Intelligence Centre

Navilas® 577 laser system for retinal laser photocoagulation

TIMEFRAME: Estimated earliest commercial availability in the UK

CE Marked

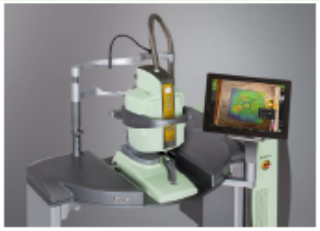
Currently unclear | Now | 6 months | 1 year | 18 months | 2 years | Over 2 years

Click here for Lay Summary

TECHNOLOGY

The Navilas® 577 laser system is a device developed by OD-OS GmbH and distributed by Instinctive Limited for treating patients who require retinal laser photocoagulation.

The technology is intended for use in the treatment of clinically significant diabetic macular oedema, proliferative diabetic retinopathy, sub-retinal neovascularisation, central and branch retinal vein occlusion, lattice degeneration and retinal tears and detachments.



July 2016

Horizon Scanning Research & Intelligence Centre

Tivantinib for unresectable hepatocellular carcinoma with high c-MET expression – second line

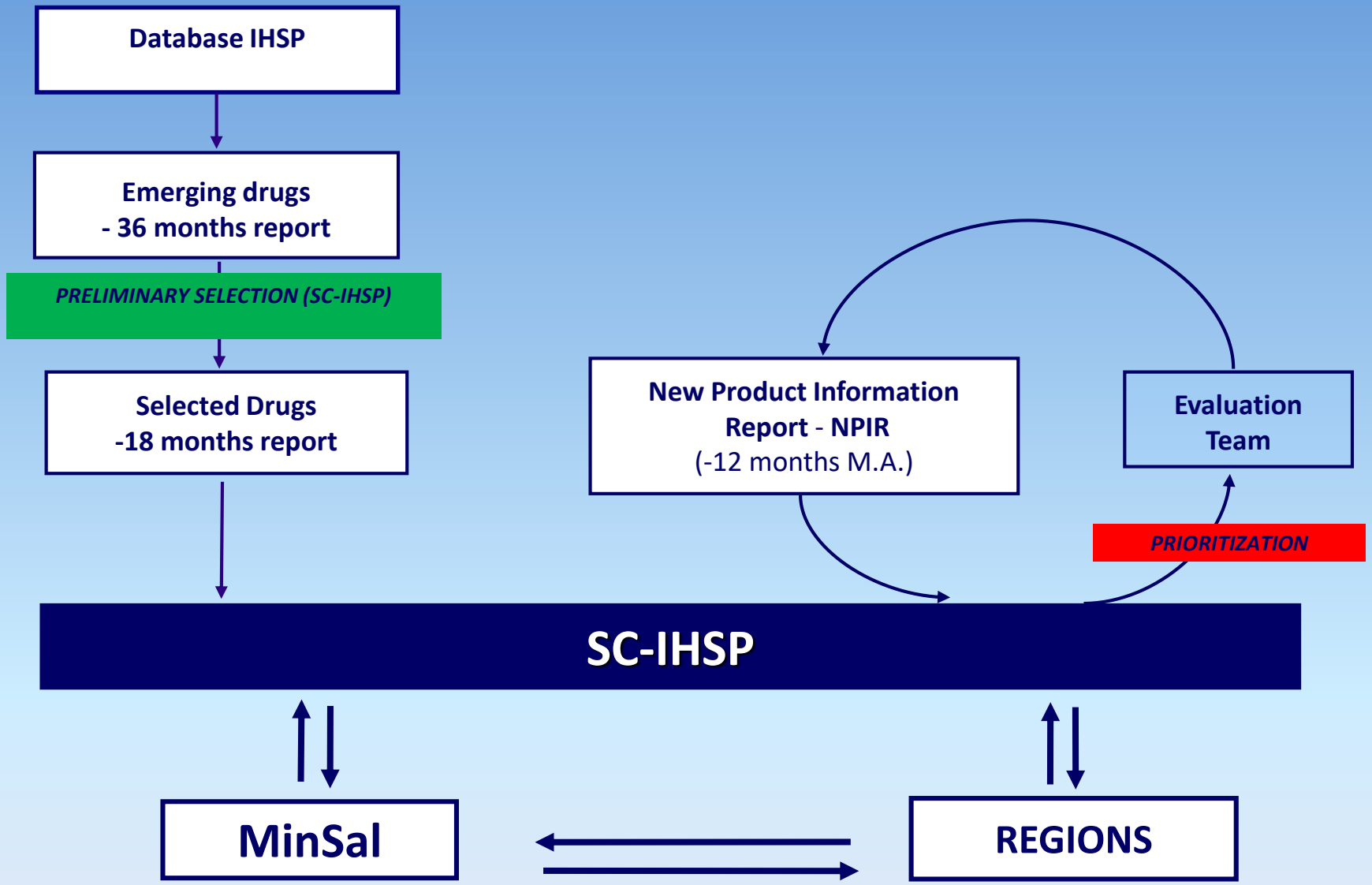
EuroScan
International Network

Horizon Scanning:
A managed introduction of emerging drugs

- ✓ To produce timeliness Assessment of emerging drugs
- ✓ To compare “real world” patients with those included into RCTs
- ✓ To identify the potential target population for the new drugs

The example of the New Anticoagulants

IHSP Workflow



New Product Information Report

Dabigatran

Stroke prevention and systemic thromboembolism in AF

PG: 03-10-2008
Update: June 2010

Summary

Clinical and Patients impact

Mechanism of action
Dabigatran etexilate is the prodrug of dabigatran, which is a potent, competitive, reversible direct thrombin inhibitor, thus preventing thrombus formation. Dabigatran also inhibits free thrombin, fibrin-bound thrombin and thrombin-induced platelet aggregation.

Efficacy
Efficacy of dabigatran etexilate has been investigated in RE-LY, a phase III, non-inferiority, randomised, active-controlled study conducted in 18,113 atrial fibrillation patients (mean age 71.5) with a history of cardiovascular disease. Patients were randomised to receive dabigatran (110 or 150 mg twice daily, double-blind use) or warfarin (1, 3 or 5 mg oral, open-label use). Incidence of stroke (including hemorrhagic) or systemic embolism (based on the time to the first event) was the primary endpoint, with a non-inferiority hypothesis of HR (dabigatran vs. warfarin) < 1.46.
After a median follow-up of 2.0 years, the annual incidence of stroke or systemic embolism for dabigatran was 1.53% in 110mg arm (n=6015, RR 0.91, 95% CI, 0.74-1.11, *p*<0.001 for non-inferiority and *p*=0.34 for superiority vs. warfarin) and 1.11% in 150mg arm (n=6076, RR 0.66, 95% CI, 0.53-0.82, p<0.001 for non-inferiority and superiority *vs.* warfarin), compared to 1.69% the warfarin group.
The annual rate of myocardial infarction were significantly more common with both doses of dabigatran than with warfarin (mean of 0.73% vs. 0.53%, RR=1.36, 0.99-1.89, p=0.06 vs. warfarin).

Safety
In RE-LY, the annual rate of major bleeding for dabigatran was 2.71% in 110mg arm (RR 0.80, 95% CI, 0.69-0.93, p=0.003 vs. warfarin) and 3.11% in the 150mg arm (RR 0.93, 95% CI, 0.81-1.07, p=0.31 vs. warfarin) compared with 3.36% per year in pts administered with warfarin.
The annual incidence of major gastrointestinal bleeding (life threatening or not) for dabigatran 150mg and warfarin, was of 1.51% and 1.02%, respectively (RR 1.50, 95% CI, 1.19-1.89, p<0.001 vs. warfarin).
During the second year, there was a higher rate of dropout with dabigatran (~21%) than warfarin (16.6%).

Innovation and/or advantages
In patients with atrial fibrillation, dabigatran should be less susceptible to dietary, drug interactions and genetic polymorphisms than its comparator warfarin. Furthermore, neither anticoagulation monitoring nor dose adjustments are necessary with dabigatran compared to warfarin.

NHS and Financial Impact

Possible price
Price of dabigatran for the new indication is not yet available.
Taking into account the ex-factory price of dabigatran for the already authorised indication in Italy, the cost of 12-month therapy should be of € 2,409 for 110 mg bid-dose and € 4,818 for 150 mg bid-dose, compared with € 26.4 for warfarin administrated at 5mg/die (INR of 2.0 to 3.0).
The price per year per person of INR analysis is € 50.35 [cost is calculated based on the labour price performed 8 times during the first month (until INR stabilization) and once per month thereafter].

Italian possible setting: Community

Possible place in therapy
The aimed indication virtually includes all the patients with non-valvular AF (those with unstable INR with warfarin or for whom INR monitoring is not convenient, those treated with antiplatelet drugs, those not treated at all, incident patients). It is likely that dabigatran will only be reimbursed for the first of these patient categories. Replacement of prevention with antiplatelet agents by dabigatran in low-risk patients is not evidence-based since there is no head-to-head comparison of dabigatran and aspirin and/or clopidogrel in AF. Patients not compliant with warfarin are even less likely to comply with the bid regimen of dabigatran. Since there is no reason to switch patients with stable INR on warfarin to dabigatran, the cheaper treatment should be tried first in de novo patients too.

Current and future indications deserve consideration: dabigatran is currently approved (and reimbursed in Italy) for the prevention of VTE in orthopaedic surgery. It is being developed for the treatment of VTE and acute coronary syndrome. The marketing authorisation application submitted to the EMA at present regards the prevention of stroke and systemic embolism in NON-valvular AF. However, patients with VALVULAR AF are at higher risk of stroke and systemic embolism and it is likely that there will be an off-label use of dabigatran in these patients.

New Product Information Report

Rivaroxaban

Stroke prevention and systemic thromboembolism in AF

PG: 17-12-2010
Update: December 2011

Summary

Clinical and Patients impact

Mechanism of action
Rivaroxaban is a highly selective direct factor Xa inhibitor with oral bioavailability

Efficacy
In ROCKET-AF (randomised, double-blind, double-dummy, non-inferiority phase III trial) 14,264 patients with AF and *CHADS2-score* ≥2 were randomised to receive oral rivaroxaban (20 mg/day) or warfarin (dose adjusted to INR 2-3). After a median follow-up of 590 days, annual rate of stroke - ischemic or hemorrhagic- or systemic embolism (primary endpoint) in PP population was 1.7 % vs. 2.2% [rivaroxaban vs. warfarin; HR 0.79, 95% CI (0.66;0.96), p<0.001 for non-inferiority]. In the safety population, annual rate of ischemic stroke was 1.34% vs. 1.42% [HR 0.94, p=0.581] and annual rate of all-cause death was 1.87% vs. 2.21% [HR 0.85, p=0.073].

Safety
Annual rate of primary safety endpoint major + non-major bleeding was 14.9% vs. 14.5% [rivaroxaban vs. warfarin, HR. 1.03 (0.96–1.11), p=0.44]. Annual rate of major bleeding (including clinically overt bleeding accompanied by a decrease in the haemoglobin level of ≥2 g/dL or transfusion of ≥2 units of packed red cells, occurring at a critical site, or resulting in death) was 3.6% vs. 3.4% [HR 1.04, 95% CI (0.90;1.20), p=0.58]. Among major bleeding, rivaroxaban augmented the annual frequency of transfusion (1.6% vs. 1.3%, p=0.04) and of decrease in haemoglobin of ≥2 g/dL (2.8% vs. 2.3%, p=0.02). During the trial, rate of treatment-emergent adverse events was 81.44% vs. 81.54% (rivaroxaban vs. warfarin). Total discontinuations were 23.7% vs. 22.2% and discontinuations due to AEs: 8.3% vs. 7.0%.

Innovation and/or advantages
Advantage of rivaroxaban over standard anticoagulation therapy (e.g. warfarin) is pharmacokinetics stability.

NHS and Financial Impact

Possible price
Price of apixaban is not yet available. One-month therapy with warfarin (dose-adjusted to INR 2.0-3.0) costs € 2.17. In addition, annual INR monitoring, according to standard laboratory protocol, costs € 50.35.

Italian possible setting: Community

Possible place in therapy
According to trial results from ROCKET-AF and considering its inclusion/exclusion criteria, rivaroxaban should become a treatment option for patients with atrial fibrillation and presenting with CHADS2-score ≥2 (with history of stroke/TIA or systemic embolism or with at least two additional risk factors of stroke among age≥75; chronic heart failure, diabetes mellitus, hypertension or risk for future stroke)

New Product Information Report

Apixaban

Stroke prevention and systemic thromboembolism in AF

PG: 17-12-2010
Update: December 2011

Summary

Clinical and Patients impact

Mechanism of action
Apixaban is a reversible, potent inhibitor of both free and cell bound factor Xa (FXa) and activated prothrombinase.

Efficacy
In the pivotal phase III, randomised, double-blind, double-dummy, non-inferiority phase III trial (**ARISTOTLE**, NCT00412984), 18,201 patients with AF and CHADS2-score≥1 were randomised to receive oral apixaban 5 mg twice daily (2.5 mg twice daily if at high risk of bleeding) or warfarin (dose adjusted to INR 2-3). After a median follow-up of 1.8 months per patient, annual rate of stroke -ischemic or hemorrhagic- or systemic embolism (primary endpoint, ITT analysis) was 1.27% vs. 1.60% [apixaban vs. warfarin; HR 0.79, 95% CI (0.66;0.95), p<0.001 for non-inferiority; p=0.01 for superiority]. Annual rate of ischemic stroke was 0.97% vs. 1.05% [HR 0.92, 95% CI (0.74;1.13), p=0.42 for superiority].
In the phase III **AVERROES** trial (NCT00496769; N=5,599), apixaban was superior to ASA in preventing stroke -ischemic or hemorrhagic- or systemic embolism (primary endpoint; ITT analysis: 1.6% vs. 3.7%, p<0.001) in patients not eligible to warfarin (CHADS2-score≥1)

Safety
In **ARISTOTLE**, annual rate of major bleeding was 2.13% vs. 3.09% [apixaban vs. warfarin, HR 0.69, 95% CI (0.60;0.80), p<0.001]. Fatal bleeding were 34 e 55 in apixaban and warfarin arms, respectively. During the trial, rate of adverse events (AEs) was 81.5% vs. 83.1% (apixaban vs. warfarin); rate of serious AEs 35.0% vs. 36.5%; discontinuations due to AEs 7.5% vs. 8.2%; total discontinuations were 25.3% vs. 27.5%.
In **AVERROES**, annual rate of major bleeding was 1.4% vs. 1.2% [apixaban vs. ASA, HR 1.13, 95% CI (0.74;1.75), p=0.57]. Rate of cardiac disorders and of gastrointestinal disorders were comparable in the two arms. During the trial, rate of serious AEs was 22.2% vs. 27.2% (apixaban vs. warfarin, <0.001); total discontinuations were 17.9% vs. 20.5%.

Innovation and/or advantages
Advantage of apixaban over standard anticoagulation therapy (e.g. warfarin) is pharmacokinetics stability, thus rendering periodic dose-adjustment not necessary.

NHS and Financial Impact

Possible price
Price of apixaban is not yet available. One-month therapy with warfarin (dose-adjusted to INR 2.0 - 3.0) costs € 2.17. In addition, annual INR monitoring, according to standard laboratory protocol costs € 50.35.

Italian possible setting: Community

Possible place in therapy
According to results from ARISTOTLE trial, apixaban should be a treatment option for patients with atrial fibrillation and at least one additional risk factor for stroke (CHADS2-score≥1), as alternative to warfarin.
According to results from AVERROES, apixaban should be also prescribed to patients with CHADS2-score≥1 but not considered eligible to warfarin therapy. Actually those patients are treated with ASA.

Possible place in therapy

Alternative to warfarin in patients with AF, untreated and with CHADS2-score≥2, or unstable (2<INR<3)

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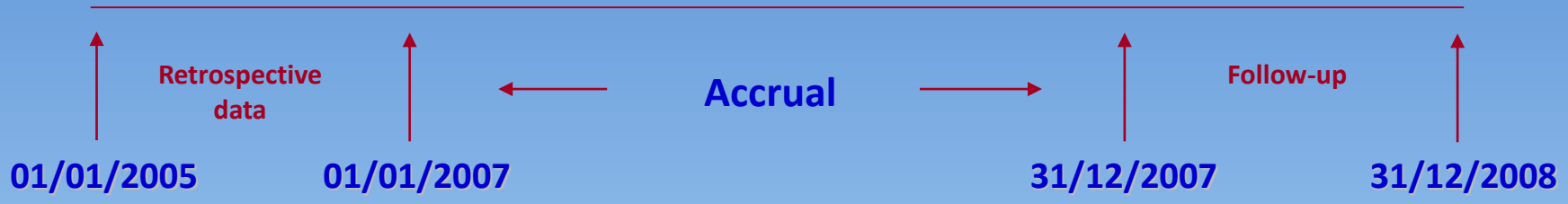
Horizon Scanning:
A managed introduction of emerging drugs

- ✓ To produce timeliness Assessment of emerging drugs
- ✓ To compare "real world" patients with those included into RCTs
- ✓ To identify the potential target population for the new drugs

The example of the New Anticoagulants

Study design



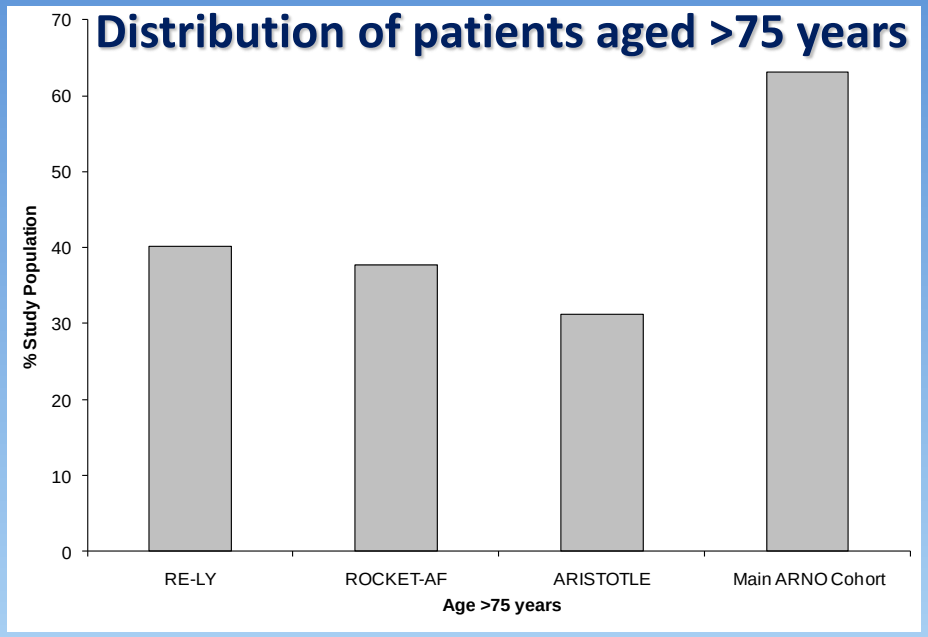
Cohort aged ≥18 years

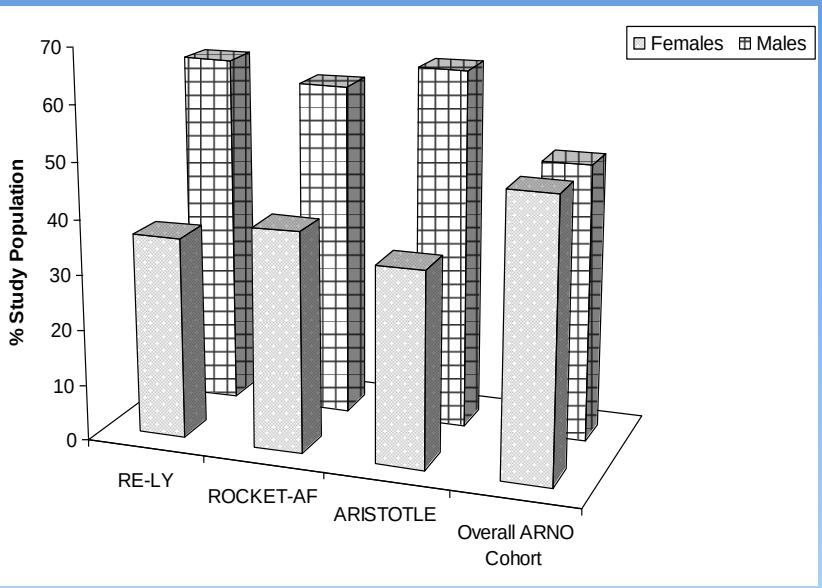
2,862,264 subjects

ARNO Cohort discharged with a diagnosis of non-valvular AF

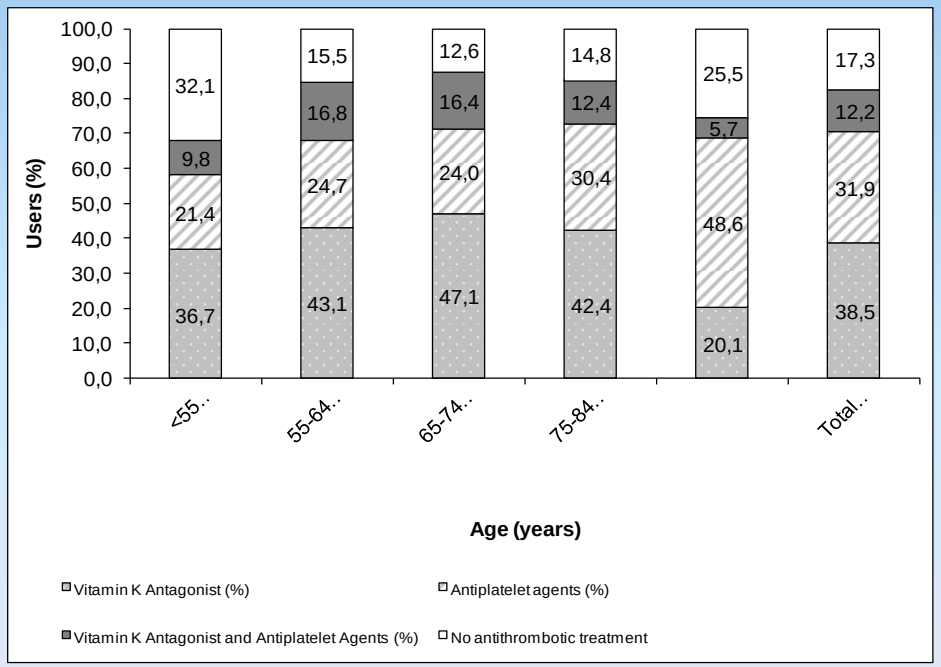
13,360 subjects

ARNO Cohort vs. RE-LY, ROCKET or ARISTOTLE Studies





Gender distribution



Prevalence of antithrombotic treatments in the ARNO cohort according to age

Horizon Scanning:
A managed introduction of emerging drugs

- ✓ To produce timeliness Assessment of emerging drugs
- ✓ To compare “real world” patients with those included into RCTs
- ✓ To identify the potential target population for the new drugs

The example of the New Anticoagulants

Proposed Criteria for the treatment with the new anticoagulants

Patients with a diagnosis of non-valvular AF, no severe renal impairment, no severe stroke in the previous 6-12 months

AND

treated with ASA or no anti-thrombotic treatment and CHADS2 score ≥2 (UNTREATED)

OR

treated with Vitamin K antagonists but unstable (2<*INR*<3)

Exclusion criteria

✓ Renal failure: 3.6% of the ARNO cohort was hospitalized in the previous 12 months

✓ Stroke: 2.2% (no inclusion into RE-LY and ROCKET-AF) of the ARNO cohort was hospitalized in the previous 6-12 months

Warnings

✓ Polipharmacy: 92.9% of the ARNO cohort treated with ≥3 associated drugs (mean 8 medicines/patient; range 1-28);

✓ Amiodarone: 20.1% of the ARNO cohort vs. 10.7% in RE-LY and 11.3% in ARISTOTLE, respectively ➡ to half the dose of dabigatran

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ARNO Cohort with non-valvular AF

13,360 subjects

Pts. hospitalized from renal failure 3.6%

Pts. hospitalized from stroke or TIA 2.2%

Potential eligible cohort

12,585 patients

UNTREATED

49.2%

UNTREATED

with CHADS2 score ≥2

62%

TREATED with

Vitamin k antagonists

38.5%

UNSTABLE (2<INR<3)

25%*

* Wallentin L. Lancet 2010 Sep 18;376(9745):975-83.

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Italian patients aged ≥18 years with non-valvular AF

716,837*

Excuded due to severe renal impairment

3.6%

Excluded due to stroke or TIA

2.2%

Potentially eligible patients

675,261

UNTREATED (49.2%)

332,228 pts

UNTREATED

with CHADS2 score ≥2 (62%)

205,981 pts

TREATED with

Vitamin k antagonists (38.5%)

259,976 pts

UNSTABLE [2<INR<3] (25%)

64,994 pts

* Health Search – ESC 2008 – Eur Heart (2008) 29 (suppl 1): 505-32

NHS sustainability

UNTREATED

with CHADS2 score ≥2

205,981 pts

UNSTABLE [2<INR<3]

64,994 pts

Eligible patients

270,975

Possible price

€2.10/die

1° year market share: 8%

€13,292,950

2° year market share: 30%

€49,848,561

Thank you for your attention from everyone in the EuroScan International Network

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