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Collaborative models for increasing efficiency of early drug assessment

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Horizon Scanning in Oncology (HSO)

Since 2009 programme line at LBI-HTA, commissioned by regional hospital providers and MoH

Aim: To identify anticancer drugs that are new (in the phase of adoption, i.e. in the launch or early post-marketing stages) or emerging (in phase III) with relevant therapeutic and financial impact

Methods: identification, filtration and prioritisation every 3 months

Outputs: about 1 – 2 assessments/every 3 months, currently 54 reports published (i.e. short about 14 pages, English)

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Evaluation

- After 3 years: evaluation (2012)
- Investment of time, effort and financial resources justified?
  - Target group, information needs?
  - Redundancies, overlaps – potential for collaboration?

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Overlaps? POP-Database

- 39 responding partners
- 1.068 projects
- 100 alert topics
- 244 similar projects within the alert topics

Agent	Agency	Agency	Agency	Agency
Nivolumab	NICE	AETSA	HIS	LBI
Pembrolizumab	NICE	AETSA	HIS	LBI
Idelalisib	NICE	AETSA	NCPE	
Afatinib	NICE	IQWiG		
Pertuzumab	NICE	Reg Veneto	HIS	ZIN

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Environmental analysis

Trastuzumab	1st-line advanced gastric cancer	10/2010	01/2010	09/2010	NHSC 09/2007 (prior to EMA approval) **LBI-HTA 05/2010 (4 months after EMA approval)** SMC 07/2010 and resubmission in 01/2011 (6 months after EMA approval) NICE 11/2010 (10 months after EMA approval) SMC 01/2011 (12 months after EMA approval) and 07/2010
Pazopanib	1st line therapy of locally advanced and/or metastatic renal cell carcinoma	10/2009	06/2010	06/2010	NHSC 04/2008 (prior to EMA approval) **LBI-HTA 10/2010 (4 months after EMA approval)** AKDAE 12/2010 (6 months after EMA approval) [1] NICE 02/2011 (8 months after EMA approval) SMC 03/2011 (9 months after EMA approval) HAS 02/2011 (8 months after EMA approval)
Ipilimumab	Pre-treated patients with advanced/metastatic melanoma	03/2011	07/2011	07/2011	NHSC 04/2008 (prior to EMA approval) **LBI-HTA 12/2010 (8 months prior to EMA approval)** NCPE 09/2011 (2 months after EMA approval) AKDAE 11/2011 (4 months after EMA approval)

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Workshop

October 2010

Since then calls for collaboration:

- about every 3 months by LBI-HTA
- Call for (co-) author(s)
- Timeframes

Agency	Country
Drug Commission of the German Medical Association (AkdÄ)	Germany
Agency for Health Technology Assessment in Poland (AHTAPol)	Poland
Health Care Insurance Board (CVZ)	The Netherlands
French National Authority for Health (HAS)	France
Institute for Pharmacology at Clinic Bremen (HTA Centre Bremen)	Germany
Institute for Quality and Efficiency in Healthcare (IQWiG)	Germany
Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA)	Austria
National Centre for Pharmacoeconomics (NCPE)	Ireland
The Norwegian Knowledge Centre for the Health Services (NOKC)	Norway
National Institute for Health and Welfare (THL)	Finland
Center for the Evaluation of Effectiveness of Healthcare of the Region of Veneto (UVEF)	Italy
Regio Veneto – ULSS20 Verona (ULSS20)	Italy

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Calls for collaboration

- 13 calls
- 16 jointly produced reports published
  - Collaboration of 6 agencies
  - 2 - 5 researchers involved/report
  - 2 - 3 agencies/report
  - Duration of assessments: ~ 3 months

Topic	Authoring agency	Collaborating partners
1. Dasatinib (Sprycel®) for chronic myeloid leukaemia	LBI-HTA	AOTM
2. Cabazitaxel (Jevtana®) prostate cancer	LBI-HTA	HTA Centre Bremen
3. Eribulin (Halaven®) for advanced/metastatic breast cancer	LBI-HTA	AOTM UVEF
4. Abiraterone acetate (Zytiga™) for prostate cancer	LBI-HTA	HTA Centre Bremen
5. Vemurafenib for melanoma	IHSP	LBI-HTA
6. Axitinib (AG013736, Inlyta®) for renal cell carcinoma	IHSP	LBI-HTA
7. Lenalidomide for myelodysplastic syndrome	LBI-HTA	UVEF AOTM
8. Ipilimumab for melanoma	IHSP	LBI-HTA
9. Lenalidomide (Revlimid®) for multiple myeloma	IHSP	LBI-HTA
10. Trametinib for melanoma	IHSP	LBI-HTA
11. Trastuzumab emtansine (KadcylaTM) for breast cancer	LBI-HTA	AOTM IHSP
12. Radium-223 dichloride (Xofigo®) for prostate cancer	LBI-HTA	AOTM IHSP
13. Obinutuzumab (Gazyva®) for chronic lymphocytic leukaemia	LBI-HTA	AOTM IHSP
14. Idelalisib (Zydelig®) for chronic lymphocytic leukaemia	LBI-HTA	IHSP
15. Nivolumab (Opdivo®) for metastatic melanoma	AKdAE	LBI-HTA
16. Nivolumab (Nivolumab BMS®) for non-small cell lung cancer	LBI-HTA	AKdAE

AOTM = Agencja Oceny Technoligii Medycznych (PL), AKdAE = Arzneimittelkommission der deutschen Ärzteschaft (D), IHSP =Italian Horizon Scanning Project, Dipartimento Farmaceutico, Azienda (IT), LBI-HTA = Ludwig Boltzmann Institute for HTA (AT), UVEF = Azienda Ospedaliera Universitaria Integrata Verona (IT)

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Different modes of collaboration

1. „Standard approach“:
   - 1 authoring agency: responsible for literature search, data extraction, compilation of first version of report
   - 1 - 2 co-authoring agency/-ies: check of literature selection/data extraction, commenting on draft
2. Sharing of products:
   - previously compiled report from collaborating agency – adaptation to HSO structure
   - collaborating agency approves HSO report

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Experiences

- Relevance of topics
- Timing
- Publication language
- Repeated collaboration increased trust/confidence in products
- Challenges with different methodology/technical issues
- Ultimately reduced work-load

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Re-use of jointly produced EUnetHTA assessments

EUnetHTA = European network (44 organisations designated by Member States + regional/non-for-profit organisations)

- to create an effective and sustainable network for HTA across Europe to help developing reliable, timely, transparent and transferable information
- support collaboration between European HTA organisations

Outputs: Production of 7 Joint Assessments on pharmaceuticals in international collaboration – Reuse/adaptation by local HTA agencies

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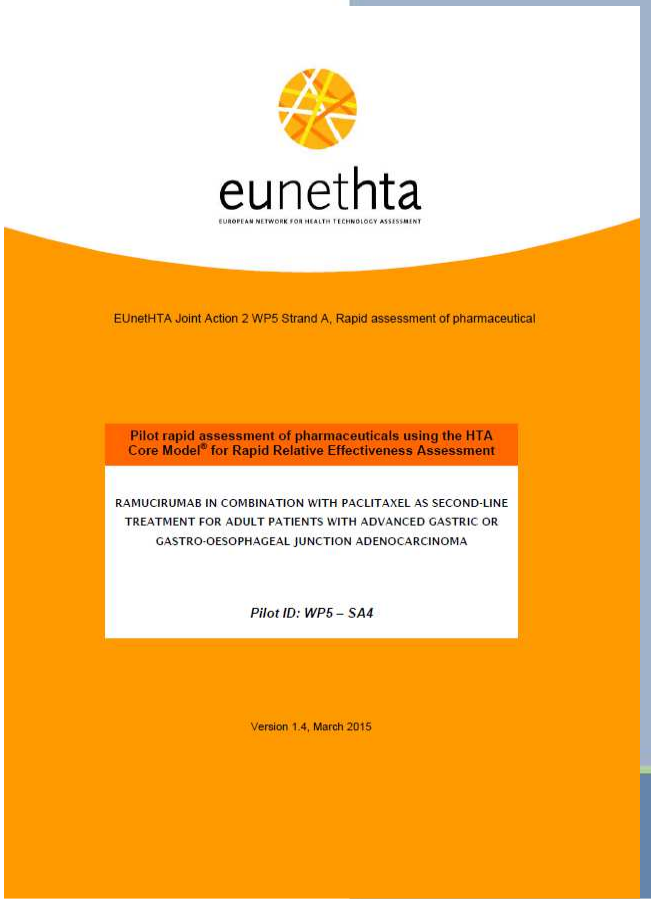
EUnetHTA
Joint Assessments

14 Joint assessments published

5 rapid assessments on pharmaceuticals:

- focus on effectiveness and safety, no economic evaluation
- within 100 days after positive CHMP decision



Adaptation of EUnetHTA assessment

„Ramucirumab for gastric cancer“:

- Adaptation of structure to EUnetHTA Core Model

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HTA Core Model Structure

EUnetHTA Joint Assessment

[A0004] What is the natural course of advanced gastric cancer or gastro-oesophageal junction adenocarcinoma?

Patients who present with advanced gastric cancer at diagnosis have a poor prognosis and expected survival times of less than a year. They typically have lymph node metastases and surgery is not considered curative (but palliative if performed) [49,51,52]. Different chemotherapy regimens can result in median PFS and OS times of several months to about a year [53-57]. This seems to depend on different prognostic factors such as Eastern Cooperative Oncology Group (ECOG) performance status, baseline haemoglobin and carcino-embryonic antigen levels, the length of time from the start of first-line treatment of the disease until disease progression, tumour localisation, number of metastatic sites, peritoneal metastases, weight loss of less than 10%, ascites, tumour differentiation, prior gastrectomy, disease status (locally advanced versus metastatic disease) and geography [1,6,58-60].

European [61] mean 5-year age-standardised relative survival for stomach cancer was 25.1%, whereas Japan [49] had better survival outcomes of around 70%, possibly due to differences in the underlying subtypes of gastric cancers, but also due to differences in the care provided [51]. Mass gastric cancer screening was introduced in Japan in the 1960s, resulting in earlier diagnosis compared with Western countries where screening to a similar extent has not so far been introduced [51,62]. About 80% of patients presenting with locally advanced gastric cancer in Japan can be cured with resection of the tumour, whereas in the West this is the case for a lower proportion (below 55%) of such patients [49].

Effects of the disease or health condition

[A0005] What are the symptoms and the burden of advanced gastric cancer or gastro-oesophageal junction adenocarcinoma for the patient?

The symptoms and burden of advanced gastric cancer for the patient commonly include fatigue, nausea, vomiting, anorexia, abdominal pain, diarrhoea or constipation, melaena, haematemesis, weight loss, and anaemia [63-67].

HSO report

3 Indication

Ramucirumab in combination with paclitaxel is indicated for the treatment of adult patients with advanced gastric cancer or gastro-oesophageal junction (GEJ) adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy. According to treatment guidelines, only patients who have a good performance status at the time of progression after first-line treatment are considered to be candidates for second-line therapy (see Scope) [4].

A0007: target population

4 Current regulatory status

In Europe, ramucirumab received orphan drug status in 2012 and market authorization by the EMA in December 2014 [5]:

- in combination with paclitaxel for the treatment of adult patients with advanced gastric cancer or GEJ adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy.

A0020: approval status

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Adaptation of EUnetHTA assessment

„Ramucirumab for gastric cancer“:

- Adaptation of structure to EUnetHTA Core Model
- Directly used + local and context-specific information
- Update of systematic search

8 working days needed for HSO report

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Conclusions

- Redundancies!
- Efficiency gains due to collaboration and re-use of joint assessments
- Harmonisation of methods (Europe/local) could further contribute to reduction of redundancies
- Topic, timing and quality key drivers!

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Further information:

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HSO Assessments:
http://hta.lbg.ac.at/page/horizon-scanning-in-der-onkologie-berichte