Disparities of Cancer Medicine Access in Europe

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Disparities in cancer outcomes (survival) across Europe

Lancet Oncol, 2013
Factors accounting for cancer outcomes disparities

Health system infrastructure

(Late) Stage at diagnosis

Cancer care infrastructure (priority devices?)

General population health and lifestyle

Disparities in cancer care

Cancer “workforce”

Patient Access & Availability of Cancer Medication
Access to cancer medication: What are the obvious problems?

- Health professionals
  - Not enough quality/benefit obtained with new strategies/drugs

- National bodies
  - Incoherent reimbursement strategy
  - Patient Access to Cancer Medication

- Pharma
  - Dramatically increased pricing
ESMO Anti-Neoplastic Medicines Survey

Perception survey to map access to cancer medicines, including WHO Essential Medicines, reporting on:

- **Approval status (yes/no) across Europe**
  - Informative for new drugs

- **Reimbursement (yes/no)**
  - Highlight differences in cancer policies
  - Residual (out of pocket) cost to patients
  - Delays in access due to special authorization

- **Actual availability**
  - Drug shortage for old drugs
  - Unavailability in the pharmacy (parallel export) for expensive drugs
Coordinating & Collaborating Partners

Coordinating Organization

- ESMO

Collaborating Project Partners

1. World Health Organization (WHO), Geneva, Switzerland
2. Union for International Cancer Control (UICC), Geneva, Switzerland
3. Institute of Cancer Policy, Kings College, London, UK
4. European Society of Oncology Pharmacists

- Breast Cancer
- Lung Cancer
- Colorectal Cancer
- Prostate Cancer
- Ovarian Cancer
- Sarcoma
- Pancreatic cancer
- Germ cell Tumors
- Renal cell Cancer
- GIST
- Urothelial Cancers
- Gastric and esophageal cancer
- Melanoma
Drug shortages affect several essential, old and inexpensive drugs (tamoxifen, doxorubicin, cisplatin, 5-FU, bleomycin...) not an issue of resources!
### WHO ESSENTIAL MEDICINES LIST 2015

**Solid Tumors**

- **UICC Task Force on EML**: UICC, Dana Farber Cancer Institute, ESMO, ASCO, SIOP, US NCI, NCCN International & others
- **New drugs, tumor-specific indications**

<table>
<thead>
<tr>
<th>Cytotoxics</th>
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<th>Hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>bleomycin</td>
<td>docetaxel</td>
<td>irinotecan</td>
<td>anastrozole</td>
</tr>
<tr>
<td>calcium folinate</td>
<td>doxorubicin</td>
<td>methotrexate</td>
<td>bicalutamide</td>
</tr>
<tr>
<td>capecitabine</td>
<td>etoposide</td>
<td>oxaliplatin</td>
<td>dexamethasone</td>
</tr>
<tr>
<td>carboplatin</td>
<td>fluorouracil</td>
<td>paclitaxel</td>
<td>leuprolrolin</td>
</tr>
<tr>
<td>cisplatin</td>
<td>filgrastim</td>
<td>rituximab</td>
<td>tamoxifen</td>
</tr>
<tr>
<td>cyclophosphamide</td>
<td>gemcitabine</td>
<td>trastuzumab</td>
<td></td>
</tr>
<tr>
<td>dacarbazine</td>
<td>Ifosfamide+mesna</td>
<td>vinblastine</td>
<td></td>
</tr>
<tr>
<td>dactinomycin</td>
<td>imatinib</td>
<td>vincristine</td>
<td></td>
</tr>
</tbody>
</table>

Adjuvant breast cancer: formulary inclusion and cost to patients - TRASTUZUMAB
Adjuvant breast cancer: availability - TRASTUZUMAB
Adjuvant breast cancer: preapproval required: TRASTUZUMAB
Adjuvant breast cancer
(Pre-approval causing >4 weeks delay): TRASTUZUMAB
Metastatic breast cancer (formulary inclusion & cost to patients)

- Capecitabine
- Vinorelbine po
- Zoledronate
- Bevacizumab
Metastatic breast cancer (formulary inclusion and cost to patients): Anti-Her2 therapy

Trastuzumab

Lapatinib

Pertuzumab

TDM-1

Legend:
- Free
- <25% Cost
- 25%-50% Cost
- Discount <50%
- Full Cost
- Not available
- No Data
Lung cancer: formulary inclusion and cost to patients: Targeted therapy

- Erlotinib
- Gefitinib
- Crizotinib
- Afatinib
Melanoma: formulary inclusion and cost to patients
Renal Cancer: formulary inclusion and cost to patients

- Temsirolimus
- Sunitinib
- Everolimus
- Pazopanib

Legend:
- Blue: Free
- Light Green: <25% Cost
- Green: 25%-50% Cost
- Orange: Discount <50%
- Red: Full Cost
- Black: Not available
- Grey: No Data
The pharmaceutical company requests marketing authorization
Evaluation by EMA (high degree of transparency!)
Approval by the European Commission

Time 0: the new drug is effective and safe – valid for whole EU

Europe explodes into 28 different countries...
The nightmare of the cancer medicines journey

- Many national commissions and expert committees-replicating at a lower level the same assessment done at the EMA stage
- A few HTA bodies
  - Working on few and weak data
  - With limited consultive value
- Fruitless sessions of negotiation, looking for creative/desperate strategies

The problem: \textit{JUSTUM PRETIUM} is utopia

- The price proposed by pharmaceutical companies is
  - dramatically increasing
  - frequently \textit{unrelated to the size of the benefit produced by the new medicine}
- Little transparency (if any) in the way the price is decided
An exploratory analysis of the factors leading to delays in cancer drug reimbursement in the European Union: The trastuzumab case

Felipe Ades\textsuperscript{a}, Chistelle Senterre\textsuperscript{b}, Dimitrios Zardavas\textsuperscript{c}, Evandro de Azambuja\textsuperscript{a}, Razvan Popescu\textsuperscript{c}, Florence Parent\textsuperscript{d}, Martine Piccart\textsuperscript{a, a}.

Fig. 1. Time periods for trastuzumab approval/reimbursement in the adjuvant and metastatic settings across European Union (EU) countries.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Setting</th>
<th>Primary outcome</th>
<th>ESMO-MCBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erlotinib vs carboplatin gemcitabine</td>
<td>1st line stage 3b/4 nonsquamous + EGFR mutation</td>
<td>PFS</td>
<td>4</td>
</tr>
<tr>
<td>Erlotinib vs Pt-based chemo doublet</td>
<td>1st line stage 3b/4 nonsquamous + EGFR mutation, crossover allowed</td>
<td>PFS, crossover allowed</td>
<td>4</td>
</tr>
<tr>
<td>Gefitinib vs carboplatin + paclitaxel</td>
<td>1st line stage 3b/4 nonsquamous + EGFR mutation, crossover allowed</td>
<td>PFS, crossover allowed</td>
<td>4</td>
</tr>
<tr>
<td>Afatinib vs cisplatin + pemetrexed</td>
<td>1st line stage 3b/4 nonsquamous + EGFR mutation, crossover allowed</td>
<td>PFS, crossover allowed</td>
<td>4</td>
</tr>
<tr>
<td>Crizotinib vs chemo</td>
<td>1st line stage 3b/4 nonsquamous + ALK mutation, crossover allowed</td>
<td>PFS, crossover allowed</td>
<td>4</td>
</tr>
<tr>
<td>Crizotinib vs cisplatin + pemetrexed</td>
<td>1st line stage 3b/4 nonsquamous + ALK mutation</td>
<td>PFS</td>
<td>4</td>
</tr>
<tr>
<td>Cisplatin pemetrexed vs cisplatin gemcitabine</td>
<td>1st line 3b/4 (nonsquamous)</td>
<td>PFS</td>
<td>4</td>
</tr>
<tr>
<td>Erlotinib vs placebo</td>
<td>Stage 3b/4 disease maintenance</td>
<td>PFS</td>
<td>1</td>
</tr>
</tbody>
</table>
### Example of using MCBS data: Renal cancer, Romania

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<tbody>
<tr>
<td><strong>Pazopanib vs sunitinib</strong></td>
<td>1st line metastatic with clear cell component</td>
<td>PFS non inferiority</td>
<td>4</td>
</tr>
<tr>
<td><strong>Temsirolimus vs interferon vs combined</strong></td>
<td>1st line poor-prognosis metastatic</td>
<td>OS</td>
<td>4</td>
</tr>
<tr>
<td><strong>Sunitinib vs interferon</strong></td>
<td>1st line metastatic</td>
<td>PFS, crossover allowed</td>
<td>4</td>
</tr>
<tr>
<td><strong>Axitinib vs sorafenib</strong></td>
<td>Previously treated metastatic</td>
<td>PFS</td>
<td>3</td>
</tr>
<tr>
<td><strong>Everolimus vs placebo</strong></td>
<td>2nd or 3rd line after TKI metastatic</td>
<td>PFS, crossover allowed</td>
<td>3</td>
</tr>
<tr>
<td><strong>Pazopanib vs placebo</strong></td>
<td>2nd line locally advanced or metastatic</td>
<td>PFS, crossover allowed</td>
<td>3</td>
</tr>
<tr>
<td>Interferon +/- bevacizumab</td>
<td>1st line metastatic with clear cell</td>
<td>PFS</td>
<td>3</td>
</tr>
<tr>
<td>Interferon +/- bevacizumab</td>
<td>1st line metastatic with clear cell</td>
<td>PFS</td>
<td>1</td>
</tr>
</tbody>
</table>
Example of using MCBS data: Melanoma, Romania

<table>
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<th>ESMO-MCBS</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ipilimumab</em> +/- glycoprotein 100 vaccine vs vaccine alone</td>
<td>Previously treated metastatic</td>
<td>OS</td>
<td>4</td>
</tr>
<tr>
<td><em>Vemurafenib</em> vs dacarbazine</td>
<td>1\textsuperscript{st} line or 2\textsuperscript{nd} line after IL-2 metastatic + BRAF V600E mutation</td>
<td>PFS and OS</td>
<td>4</td>
</tr>
<tr>
<td><em>Trametinib</em> vs dacarbazine or paclitaxel</td>
<td>Unresectable or metastatic + BRAF V600E mutation</td>
<td>PFS (crossover allowed)</td>
<td>4*</td>
</tr>
<tr>
<td><em>Dabrafenib</em> +/- trametinib</td>
<td>1\textsuperscript{st} line unresectable or metastatic + BRAF V600E mutation</td>
<td>Toxicity, PFS</td>
<td>4</td>
</tr>
<tr>
<td><em>Dabrafenib</em> vs dacarbazine</td>
<td>1\textsuperscript{st} line unresectable or metastatic + BRAF V600E mutation</td>
<td>PFS (crossover allowed)</td>
<td>4</td>
</tr>
</tbody>
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Example of using MCBS data: Breast cancer, Romania

<table>
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</thead>
<tbody>
<tr>
<td>Chemotherapy +/- trastuzumab</td>
<td>(Neo)adjuvant HER-2 positive tumours</td>
<td>DFS</td>
<td>A</td>
</tr>
<tr>
<td>T-DM1 vs lapatinib + capecitabine</td>
<td>2nd line metastatic after trastuzumab failure</td>
<td>PFS and OS</td>
<td>5</td>
</tr>
<tr>
<td>Trastuzumab + chemotherapy +/- pertuzumab</td>
<td>1st line metastatic</td>
<td>PFS</td>
<td>4</td>
</tr>
<tr>
<td>Lapatinib +/- trastuzumab</td>
<td>3rd line metastatic</td>
<td>PFS</td>
<td>4</td>
</tr>
<tr>
<td>Capecitabine +/- lapatinib</td>
<td>2nd line metastatic after trastuzumab failure</td>
<td>PFS</td>
<td>3</td>
</tr>
<tr>
<td>Eribulin vs other chemotherapy</td>
<td>3rd line metastatic after anthracycline and taxane</td>
<td>OS</td>
<td>2</td>
</tr>
<tr>
<td>Paclitaxel +/- bevacizumab</td>
<td>1st line metastatic</td>
<td>PFS</td>
<td>2</td>
</tr>
<tr>
<td>Exemestane +/- everolimus</td>
<td>Metastatic after failure of aromatase inhibitor (with PFS &gt; 6 mth)</td>
<td>PFS</td>
<td>2</td>
</tr>
</tbody>
</table>
**Collaborating Partners** (international study): USA, South America, Japan, China, Korea, India, Malaysia, Thailand, Australia, New Zealand, etc.
What are the solutions to improve cancer medicine access?

Health professionals

Care about benefit: Magnitude Of Clinical Benefit Scale

Patient Access to Cancer Medication

Reimburse the reasonable medicines (public policy)

National bodies

Pharma

Justum Pretium
Conclusions

- Disparities exist across Europe in access to cancer medicines
- Drug shortages affect several “essential”, old and inexpensive drugs
  - THIS SHOULD BE UNACCEPTABLE!
- Inequalities exist in availability and patient costs, especially for newer, more expensive drugs, across Europe
- The ESMO Magnitude of Benefit Scale, applied on the availability data (ESMO Antineoplastic Medicines Survey) can inform the process of prioritization access to medicines, when resources are limited