Innovation and trends in early diagnosis and treatment in Oncology

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Uppsala Health Summit

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Multiple factors contribute to drug healthcare expenditure

Total drug and non drug healthcare expenditure has risen above GDP since 1960s

Factors influencing oncology drug prices

- Lengthy R&D process
- Complexity of disease
- Registration in late stage disease

Relative Increase in Health Care Expenditure* (indexed to prior decade expenditure)

Greater chance of success and potential for quicker registration

Improved understanding of biology and drugs

Targeting precisely

Greater potential for cure

Improved long term survival

Platform studies: Evaluate multiple assets/combinations

Improved diagnostics & alternative clinical end-points

Strong signal: Potential to move fast to Ph3

Oncology, IMED Biotech Unit
Precise targeting and smart study design gives the highest chance of success

Significant improvement in PFS with osimertinib in 1st line EGFRm NSCLC (FLAURA)\(^1\)

Demographics driving study design\(^2\)

Higher prevalence of patients with EGFR mutations in Asian demographic

2. https://www.tagrisso-global.com/
Early detection and effective treatment can improve outcomes

Early stage lung cancer has improved 5 year OS

- 56% Localized
- 28% Regional
- 4% Distant

5yr overall survival

- Higher 5 year survival rate
- Potential for increased impact of treatment on long term outcome

Detection of early-stage disease positively impacts survival in breast cancer

Use of mammography among women (Age 40+) & breast cancer mortality rate*

*Source: Coverage ratio adapted from CDC, 2017; Mortality rate adapted from National Cancer Institute, 2017

Note: Coverage ratio is the percentage of women who had a mammogram within the past 2 years from the total eligible population; numbers are age adjusted.
Cost effectiveness of cancer drugs is greater in early stage

Example: Her 2 targeted antibodies

<table>
<thead>
<tr>
<th></th>
<th>Metastatic BC</th>
<th>Early BC</th>
<th>Lifetime$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICER (2006 $)</td>
<td>$85,700/QALY</td>
<td>$26,400/QALY</td>
<td>$35,600/QALY</td>
</tr>
</tbody>
</table>

1: EU label results cited: FDA label based on ITT population
2: From Garrison and Veenstra Value in Health 2009
Screening could shift treatment to early disease

Durvalumab: the 1st new treatment in 15+ yr in unresectable Stage 3 NSCLC

PACIFIC study

Predicted stage shift by 2028 by screening high risk populations in the US

1. if continued at current levels (4% of eligible patients)
2. if increased to levels similar to breast cancer (40%)

<table>
<thead>
<tr>
<th></th>
<th>Today</th>
<th>2028 screening @4%</th>
<th>2028 screening @40%</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Stage I - II</td>
<td>Stage III</td>
<td>Stage IV</td>
</tr>
<tr>
<td></td>
<td>34%</td>
<td>19%</td>
<td>48%</td>
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</tbody>
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<table>
<thead>
<tr>
<th>No. of Events/ Total No. of Patients</th>
<th>Median PFS (95% CI)</th>
<th>12-Mo PFS (95% CI)</th>
<th>18-Mo PFS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Durvalumab 214/476</td>
<td>16.8 (13.0-18.1)</td>
<td>55.9 (51.0-60.4)</td>
<td>46.2 (37.7-50.5)</td>
</tr>
<tr>
<td>Placebo 157/237</td>
<td>5.6 (4.6-7.8)</td>
<td>35.3 (29.0-41.7)</td>
<td>27.0 (19.9-34.5)</td>
</tr>
</tbody>
</table>

PACIFIC study

Oncology, IMED Biotech Unit
ctDNA plasma testing: a cost-effective test with demonstrated utility for EGFR T790M testing

Cost-effectiveness of plasma biopsy

Cost of biopsy + EGFR testing

Plasma ctDNA companion diagnostic

Plasma EGFR disease monitoring

Osimertinib (EGFRi)

Thress K et al. ASCO 2017 (Abs #9018)
Potential for ctDNA to detect Minimal Residual Disease

Post-Treatment Landmark ctDNA Predicts for Recurrence/OS in Stage I-III Lung Cancer

Post-Treatment ctDNA Predicts for DFS in Early Stage Breast Cancer
ctDNA: a game changer for oncology drug development

Minimally invasive, low risk, & amenable to frequent sampling

Patient selection  
Disease monitoring  
Acquired resistance  
PD biomarkers

Metastatic setting  
Minimal residual disease  
Early setting  
Screening

Diagnostics must be highly specific and highly sensitive

A challenging source of DNA

Dilute / low amounts of tumour DNA shedding, germline contamination
Highly fragmented DNA
Short half-life (until purified)
Sampling methods immature / variable

Oncology, IMED Biotech Unit
Wide-spread adoption of ctDNA for tumour testing might represent a win-win-win for patient, payer, and pharma

<table>
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<tr>
<th>Patient</th>
<th>Payer</th>
<th>Pharma</th>
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</table>
| • Earlier diagnosis  
• Less invasive test  
• Precision medicine  
• Early confirmation that treatment is having an effect | • Cost effective testing  
• Reimbursement directed towards patients who benefit  
• Higher cost-effectiveness for drugs in early stage disease | • Better decision-making in drug development  
• Earlier endpoints in clinical trials  
• Smaller, faster trials to get to early stage setting |

Greater chance of success