STRATIFIED MEDICINE

HOW WILL IT IMPACT BIOPHARMA COMMERCIALIZATION?

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September 2014
**Stratified medicine**

**Definition:** “The ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a particular treatment”

(ABPI White Paper 2009)

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**Personalized medicine**

**Definition:** “The potential to use biomarkers for identifying patients that are more likely to benefit or experience an adverse reaction in response to a given therapy”

(Trusheim et al, Nature Reviews 2007)

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STRATIFIED MEDICINE: A STEP CLOSER TO PERSONALIZED MEDICINE

• Using specific clinical features, biomarkers, or genetic information, stratified medicine enables clinicians to identify subgroups that have a higher probability of responding to treatment.

• Clinicians can reduce heterogeneity in patient response by reducing the reliance on mean response across large patient populations.
WITH SMALLER PATIENT POPULATIONS, EVIDENCE CAN BECOME MORE FOCUSED & STRONGER

• A predictive diagnostic test stratifies the patient population to responders and non-responders for a certain treatment

• Since treatment is focused in patients that have the greatest probability of response, clinical trials can show a greater mean effect

• Instead of showing incremental improvements, biopharma can show a large shift in efficacy in targeted subpopulations

• In addition to improved efficacy, stratification can result in reducing patient exposure to ineffective drugs resulting in a reduction in avoidable adverse events

The ultimate outcome is improved confidence of regulatory authorities in sanctioning earlier approvals
STRATIFIED MEDICINE INTRODUCES TECHNICAL CHALLENGES AND OPPORTUNITIES…

• While reduced response heterogeneity increases statistical power, subgrouping reduces sample sizes
  • Eventually, this will make traditional, large trial-based efficacy analyses impossible
• The interaction of different biomarkers increases the number of subgroups rapidly
  • Eventually, this becomes near-personalized medicine
• This requires statistical modelling of biomarker interaction

<table>
<thead>
<tr>
<th>Biomarker 1</th>
<th>Biomarker 2</th>
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</thead>
<tbody>
<tr>
<td>Low</td>
<td>Present</td>
</tr>
<tr>
<td>Medium</td>
<td>Subgroup A</td>
</tr>
<tr>
<td>High</td>
<td>Subgroup B</td>
</tr>
<tr>
<td></td>
<td>Subgroup C</td>
</tr>
</tbody>
</table>

Response = Bm1 + Bm2 + Bm1 x Bm2
As therapies become more specialized, the market tends to decrease.

Eventually, this can make new treatments uneconomical.

It can also make current reimbursement systems inefficient.

Traditionally, smaller populations have resulted in higher prices.

That is not sustainable in the long-term.

Solving this requires commercial solutions.

For example, targeted populations, but across multiple indications.
EXCLUSIVITY PERIODS CAN BE USED MORE EFFICIENTLY, INCREASING RETURN ON INVESTMENT

• Stratified medicine will enable biopharma to commercialize products faster from conception to patient uptake, especially in areas of high unmet need.

• This improved efficiency in the product development and launch cycle should result in a greater amount of time before loss of exclusivity, and potentially a larger return on investment.

• Healthcare governments will be able to support a broader range of therapies because of the increased differentiation of new therapies to established standards of care.

• Ultimately, reimbursement agencies will evaluate subpopulation focused treatments with a smaller evidence base while continuing to encourage access to new and innovative medicines.
The future success of stratified medicine is intrinsically related to the ability of diagnostics and biomarkers to identify patient subgroups.

With diagnostics teams waiting for proof of efficacy before further investments in technology, diagnostic/biomarker and drug can negotiate regulatory and reimbursement hurdles at different times.

As the complexity of these diagnostics and biomarkers increases with greater numbers of strata, the challenge may be to align reimbursement negotiations of the drug and diagnostic/biomarker test.

Although payers would be keen to reimburse a diagnostic/biomarker test to contain costs and limit budget impact, if the companion diagnostic/biomarker is not be available during drug reimbursement negotiations, efficiencies gained during early approval will be lost.
FINALLY, STRATIFIED MEDICINE COULD INTRODUCE SOME VALUE-BASED PRICING METHODS

- Early marketing authorization allows drugs to be available with a limited evidence base
  - This requires new analytic approaches
  - It may also require that prices adapt as data becomes available, in order to:
    - Support early access
    - Prevent loss of revenues due to early access
- Adaptive licensing for breakthrough products may play a significant role in the commercialization process
  - The trade off will be between earlier access for some patients versus an increased level of uncertainty around acceptable benefits
  - Evidence gathering will need to be iterative through adaption of the market authorization to allow broader patient populations to access the medicine
THANK YOU