



## EDITORIAL

# Precision medicine: do not neglect the hurdles

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**T**remendous expectations have been connected with precision medicine in the past years. Beside the advantages that this type of therapy offers we should be aware of its challenges too. In this issue we will highlight on specific challenges that the pharmacological industry is opposed with when developing new targeted therapies. In addition, we will discuss issues with the reproducibility of published scientific data.

## Precision Medicine for the Pharmacological Industry — Curse or Blessing?

The approach of precision medicine allows for the prevention and treatment of diseases, taking the huge biological variability into account, though yielding more precise treatment strategies for individuals<sup>[1]</sup>. Indeed, the clinical evidence supports the validity of this concept now being used for decades, in blood typing to guide blood transfusions, with the most recent molecular genome decoding approaches directing modern oncological therapies<sup>[2]</sup>. More drugs with biomarker determination either for efficacy or for side effect prediction are being approved. In the EU approximately 50 drugs, and in the US 100 have been approved so far. Thus the clinical value of precision medicine for patients and physicians is undeniable. For ‘the third participating party’ in the arena of precision medicine, the pharmacological industry, the introduction of targeted therapies came along with several advantages but also some challenging aspects too.

Reduced attrition in the clinical development phase by the selection of patients with a chance for a

maximal clinical response may lead to drug approval at least for a smaller cohort, in contrast to no approval at all. Since the assumed effect size should be higher when tested in patients with a higher possibility to respond, smaller study size is needed and faster conduction of the studies may result in decreased costs for the clinical development. Finally, the opportunity to achieve a high price is increased for a drug with an outstanding efficacy.

On the other hand, the cost-effective identification and development of reliable biomarkers and their assays increases further the already high costs of pre-clinical development of new drugs. The overall complexity of drug development is maximized due to necessary co-development of the drug and biomarker. Moreover, the essential skills and knowledge for co-development does not usually exist in stand-alone pharma, necessitating complex cooperation strategies. Identification and selection of suitable patients for a particular therapy, i.e., stratification, leads to the exclusion of other patients with the disease, leading to smaller populations to be treated and subsequently reducing the market size.

When comparing the advantages and challenges of precision medicine, in our view, the advantages outweigh the challenges and from an ethical perspective it seems mandatory to exclude patients from treatments which might not fare well (Table 1).

Since we are convinced that precision medicine is the future treatment, we believe the importance of the critical discussion of all aspects of precision medicine: scientific, medical, and economical for better or for worse. With our journal we would like to provide a

**Table 1.** Advantages and challenges of precision medicine from a business perspective

Advantages	Challenges
<ul style="list-style-type: none"> <li>• Reduced attrition in clinical development by selection of patients with a maximal possible chance to respond</li> <li>• Smaller study size and lower development costs in clinical development based on a smaller population to be treated to demonstrate a clinical effect</li> <li>• Opportunity to achieve a high price for a drug with major efficacy</li> </ul>	<ul style="list-style-type: none"> <li>• Additional cost to identify and validate biomarkers and assays</li> <li>• Higher project risk due to simultaneous approval of two components: the drug and the diagnostic kit</li> <li>• Loss of autonomy for pharma companies as a partner for the biomarker assay is needed</li> <li>• Smaller market size by a label restricted to biomarker positive patients only</li> <li>• Exclusion of biomarker negative patients who may have a (low) chance to gain from the therapy in some cases</li> </ul>

fruitful forum for controversial discussions.

We are highly honoured that two outstanding managers from the pharma industry, namely Professor Björn Wallmark (Astra Zeneca)<sup>[3]</sup> and Professor Günter Stock (past Schering AG)<sup>[4]</sup>, contributed their views regards precision medicine with special focus from the pharma industry to this volume.

### Are the Published Data Reliable?

Successful targeted therapies require well validated biomarkers. Usually the idea and first hints for promising biomarkers come from scientific publications. A few years ago we started a discussion on how reliable published data is. When analysing the reproducibility rate for studies investigating drug targets, we were surprised that only approximately 30% of the experiments were reproducible from the publications<sup>[5]</sup>. When looking at biomarkers, the results may be similar (unpublished observation). In line with this, there is a considerable discrepancy between the number of biomarkers identified and reported in the literature (~150,000) as well as the very few (~100) used in the daily practice<sup>[6]</sup>. Major efforts are needed to increase reproducibility in general. We are very pleased to publish in this issue two interesting articles highlighting initiatives in this area written by Dr Bhullar<sup>[7]</sup> and Dr Bespalov<sup>[8]</sup>, who are outstanding experts in this field, respectively. Another element to tackle this problem is closer collaboration, as we started to discuss in the first issue<sup>[9]</sup> and which we continue to address here<sup>[10]</sup>.

### Call for Papers

After the successful pilot issue we published six months ago, we would like to thank all authors, reviewers, the editorial board members and the publisher for the support enabling this promising start. We would like to close with a call for papers. Please feel free to submit your manuscripts, in the form of reviews, perspectives or original articles. Submission of reports with negative data as well as confirmatory va-

lidation studies is encouraged. Let's continue to make APM an attractive platform for discussions in the exciting area of precision medicine and biomarkers.

### Conflict of Interest and Funding

LL has no conflict of interest to declare. PC is an employee and shareholder of Bayer AG. KA is a shareholder of Bayer AG.

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