

Scientific Advice with HTAs

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ISSUE PANEL 13:
IT IS ALWAYS TOO EARLY UNTIL IT IS TOO LATE: WHAT CAN WE LEARN FROM THE PILOTS OF MULTI-STAKEHOLDER CONSULTATIONS IN EARLY-STAGE DRUG DEVELOPMENT?
2020-1491 - Annual European Conference - 18/05/2021 (08-11-2021)

Experience so far

- 11 procedures, 5 finalised, 5 ongoing. 1 in presubmission stage
- Diabetes, Heart Failure, Alzheimer's, Lung Cancer, Breast Cancer, Melanoma, Asthma, Rheumatoid Arthritis. Multi-resistant Infections, Food Allergies
- All new mechanisms of action in the respective area, new monoclonals, new chemicals, tumour vaccines
- HTAs and payers from Sweden, UK, France, Italy, Netherlands, Spain, Germany

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When - early

- Very early with non-clinical proof of concept and no clinical data:
- Only general responses but Company can benefit from orientation of what would be needed and the multistakeholders view on the pharmacological concept and general study design.
- A red light can be as useful as a green light (companies reflection)

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When - later

- When exploratory clinical data are available:
- Precise responses on which end-points, duration, comparators, size of the trial and statistical plans are important for the stakeholders.
- Precise idea on what / how much is required and what is feasible

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Useful? Shared discussions

- Cardiovascular death and number of rehospitalisation can be included in the same trial as endpoints
- What is the value of MRI imaging as indicator of progression of atherosclerosis?
- If cardiovascular events cannot be provided for diabetes preauthorisation what alternatives are there for the company from the Regulators and HTA point of view?
- Is this an acceptable approach to qualify circulating tumour cells as prognostic markers for progression free survival or overall survival from the Regulators and HTA point of view?

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Useful? Shared discussions

- Is this an acceptable approach to qualify circulating tumour cells as prognostic markers for progression free survival or overall survival from the Regulators and HTA point of view?
- Value of a new not validated endpoint from the Regulators and HTA point of view? E.g. Radiographic Progression free survival to include bone events in breast cancer as compared to the standard PFS per RESIST which does not include bone events

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Useful? How many participants

- High number of participants reflect a broader perspective but
- Small number of participants may facilitate a deeper, more comprehensive discussion

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Tips – Personal Reflections

- Some applicants kept the application very high level and short considering the variable back ground of the many stakeholders: not advisable, all stakeholders were of the view that comprehensive submission of the scientific facts is beneficial for the discussion and ultimately for the feedback to the applicant
- When coming early make it clear that questions are for the proof of concept experimental level and not for the confirmatory study aimed to establish benefit/risk and added value!

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Tips – Personal Reflections

- All participants understand that we have to work with a higher degree of assumptions at this stage than we are used to at Regular Scientific advice of the CHMP or discussions with HTAs but it is advisable to keep a balance between assumptions and facts in a submission otherwise there is a risk to jeopardise a good proposal

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Can all questions be shared among stakeholders?

- No but all questions can be part of the same application even if (examples):
- Are the proposed statistical approaches x/y/z to address the issue of missing values acceptable? To be answered by Regulatory statisticians only
- Is the proposed cost-effectiveness approach acceptable for reimbursement discussions? To be answered by HTA experts only

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Take home message

- Even if the parallel procedure with HTAs and regulators is more complicated than a SA with Regulators only, it can be a much more useful and efficient way to receive feedback from many stakeholders. This will enable the company to decide on clinical trial designs in terms of endpoints, duration and comparators and channel resources efficiently
- Even if not all participants provide written responses the applicant gets the messages in the extended face-to-face meeting which is always guaranteed

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