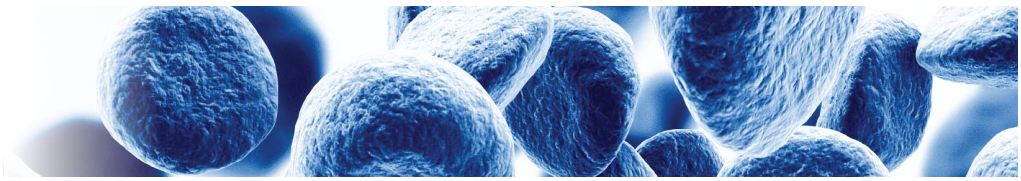

ISCT Annual Meeting 2016 (Abstract P238)

Application of Quality by Design in allogeneic cell-based therapy processes and assay development

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Introduction: The experimental original manufacturing process of ATIR101, a personalized T-cell immunotherapeutic, required significant re-engineering in order to increase process robustness, scalability and compliance with GMP environment.
Key components of Quality by Design (QbD) were integrated to guide the development of the manufacturing process and the release assays.

Material and Methods: QbD is a systematic approach to drug development, which begins with predefined objectives, and uses science and risk management approaches to gain product and process understanding and ultimately process control.

Results: A target product profile (TPP) was identified together with corresponding critical quality attributes (CQA) that define the product; also desired quality attributes (DQA) were defined to select between process optimization steps yielding similar CQAs.
Next, the manufacturing process was split into distinct unit operations and for each unit operation 3 risk assessments were done:

1. A Failure Mode and Effect Analysis (FMEA).
2. A process variability analysis
3. A sustainability analysis

These outcomes were then used to establish the priority of development and identified the crucial parameters that need to be controlled within as unit operation to yield a product that meets its CQAs.

Conclusion: Integration of key elements of QbD to guide the development of our personalized cell based medicinal product has resulted in a scalable and robust manufacturing process. Early incorporation and adoption of the QbD approach in process development will minimize risks of development failures and speed up rational process development to provide cell-based products in quality and quantity needed to comply with regulatory and market requirements.