Sandra Ribes
Sandoz Global Development
16th EIP Symposium

A retrospective analysis of clinical immunogenicity data: time for singlicate change?

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Background

- Immunogenicity testing in biosimilar development
- (Technical) duplicate vs singlicate analysis
- Health Authority requirements/expectations

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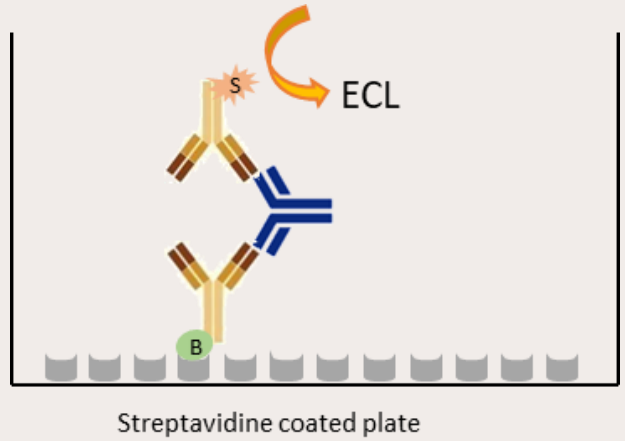
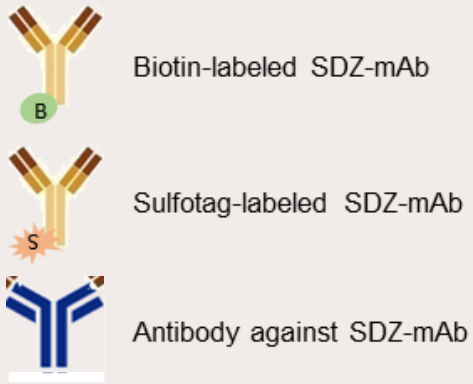
Case study

- Monoclonal IgG1 antibody biosimilar (SDZ-mAb)
- Single dose PK study in HV
  - Primary endpoints: Cmax, $AUC_{0\text{-}inf}$, and $AUC_{0\text{-}360}$
  - Safety and immunogenicity as secondary endpoints
- ADA Assay:
  - MRD 1:2
  - Sensitivity <100 ng/mL
  - LPC: ~ 100 ng/mL
  - Adequate drug tolerance





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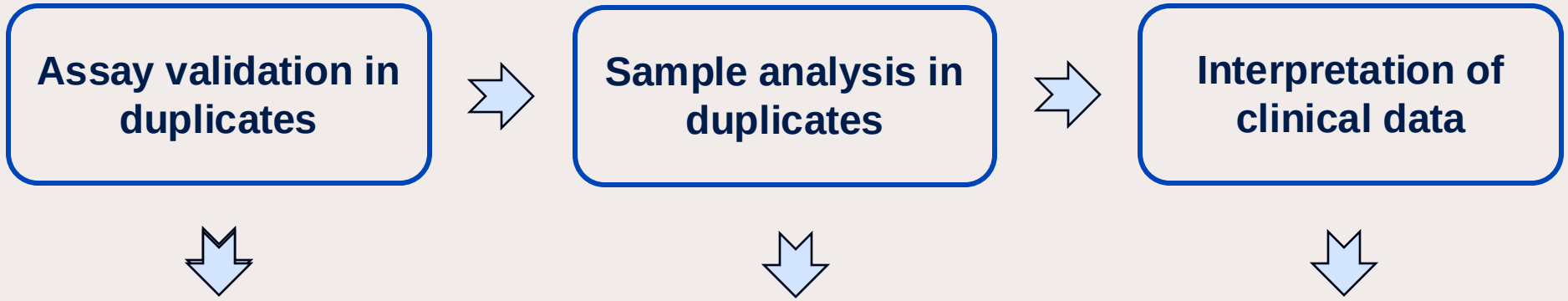
Evaluation of clinical immunogenicity



All parameters met the acceptance criteria

Screening, confirmation, titration of ADAs Characterization

~3,200 clinical samples

Assessment of clinical impact of immunogenicity on drug exposure

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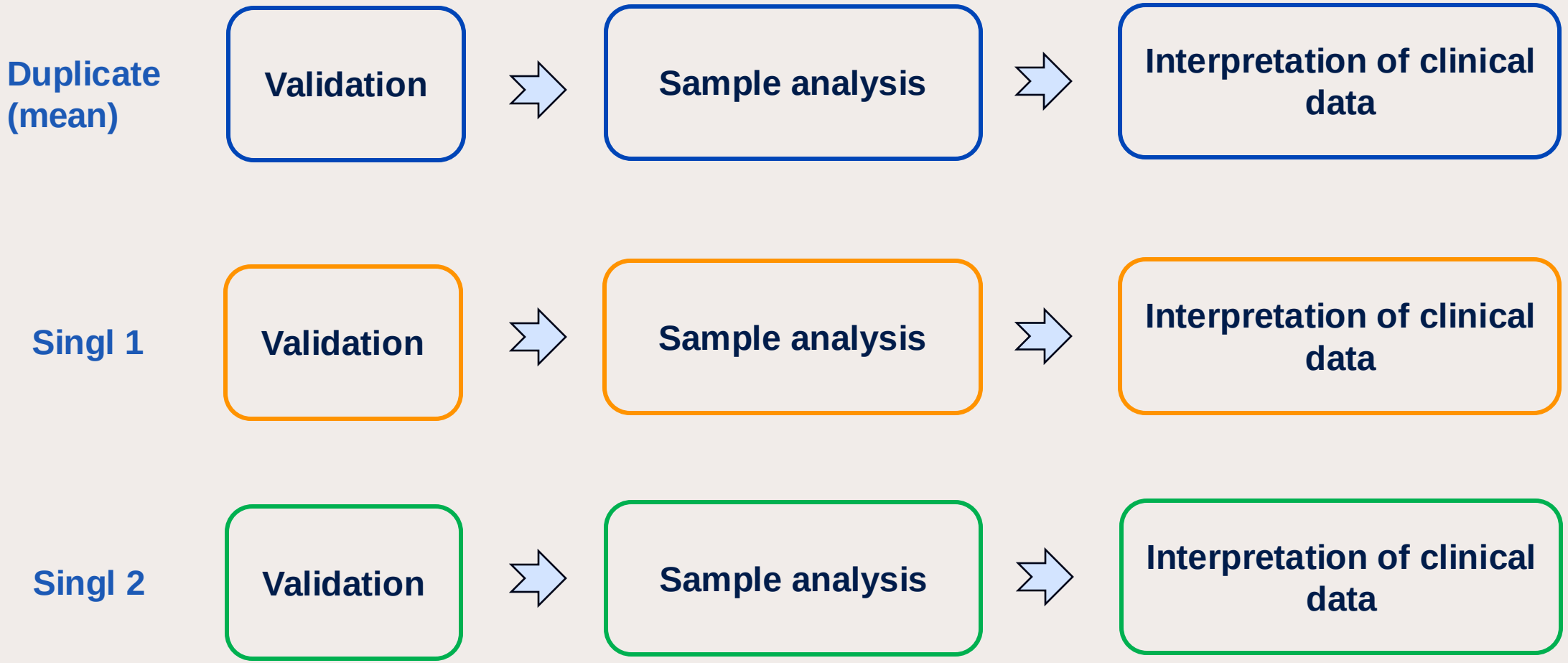
Retrospective evaluation of clinical immunogenicity



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Comparability of singlicate to duplicate in Assay Validation

Cut-points for ADA method based on duplicate and singlicate values

	Duplicate	Singlicate 1	Singlicate 2
Screening CP	1.15	1.19	1.16
Confirmatory CP	18.9%	20.4%	20.9%
Titer CP	1.27	1.32	1.29

CP: cut-point

Precision of ADA method validation using duplicate versus singlicate data

	Duplicate	Singlicate 1	Singlicate 2
Intra-assay precision (%CV)	3-8%	4-10%	3-9%
Inter-assay precision (%CV)	5-6%	4-6%	6-7%

CV: coefficient of variation

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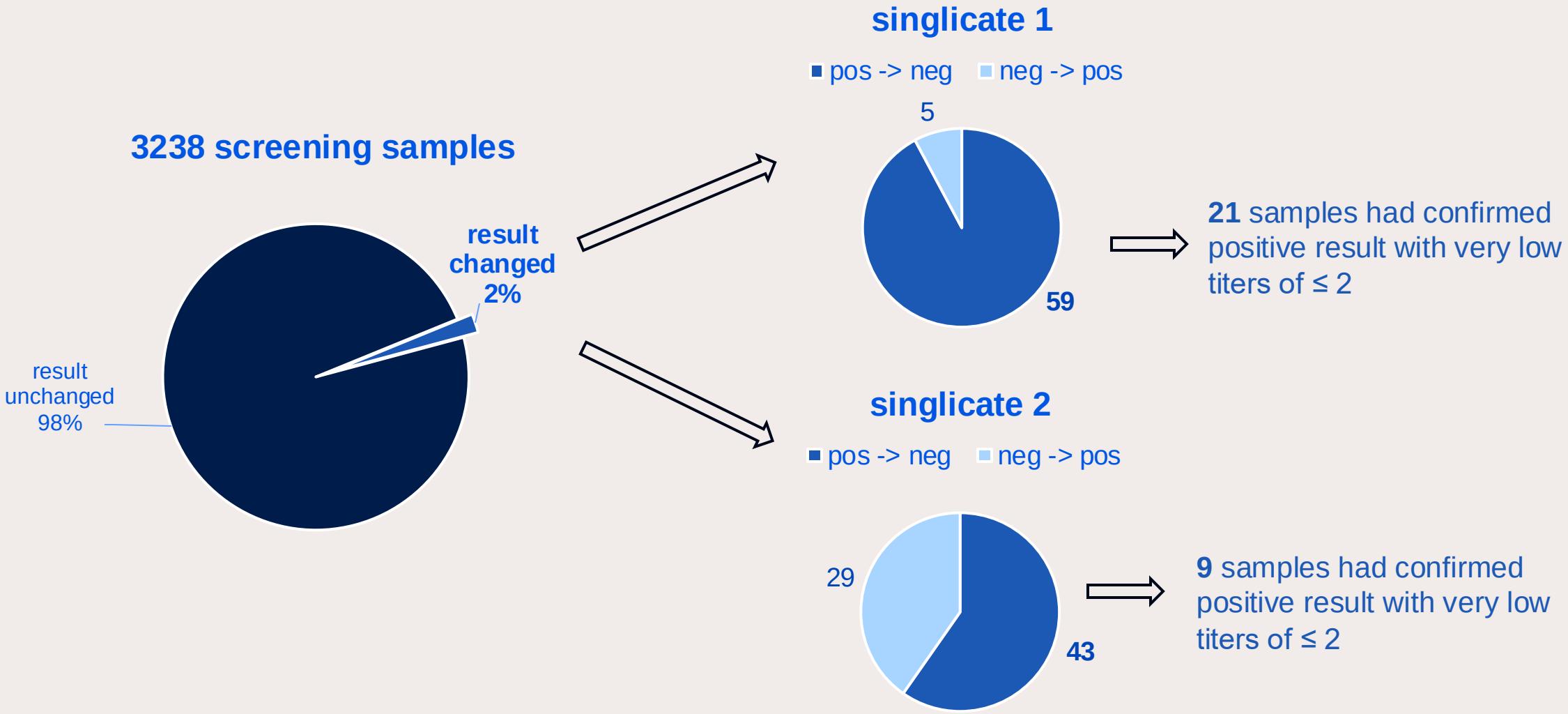
Comparability of singlicate to duplicate in Sample Analysis



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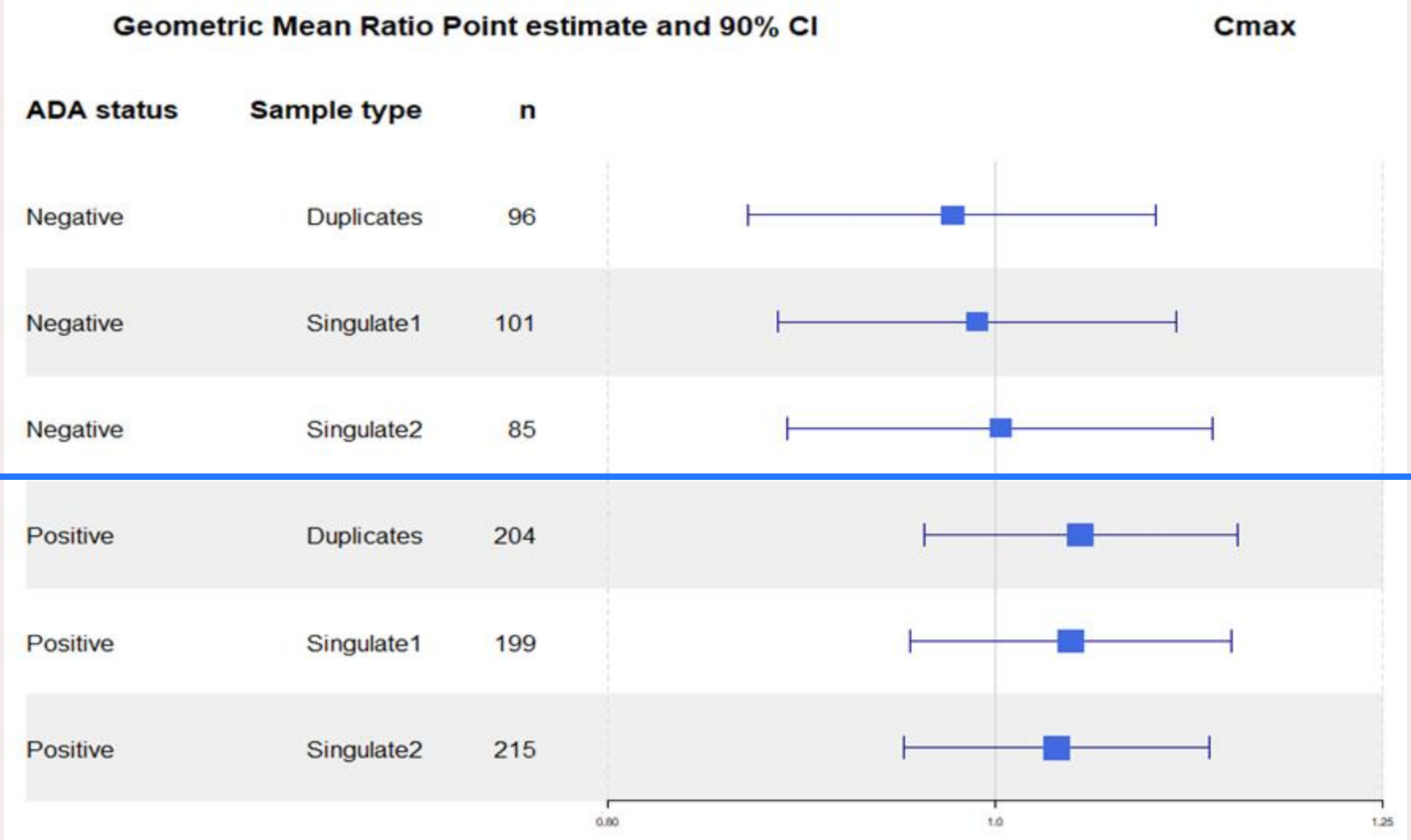
Retrospective evaluation of clinical immunogenicity



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Conclusions

- A singlicate-based ADA assay:
  - would have been equally suitable for method validation based on assay performance
  - would have delivered similar clinical immunogenicity data
  - would have delivered the same interpretation of the impact of immunogenicity on drug exposure
- **All together, ADA singlicate analysis would have been adequate to show comparable immunogenicity in our biosimilar program**
- Additional evaluation of clinical immunogenicity data from other biosimilar programs is ongoing

The team

Maike Lichtenfels

Jamie Fan

Davide Guerrieri

Mathias Hackl

Katja Jacobs

Ana Villalba Izquierdo

Thank you

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