

Computerized Algorithm for Multiple Myeloma using IMWG-2016 Response Assessments

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Agenda

- Background
- Overview of the algorithm
- Algorithm in details
- Validation
- Conclusion
- Questions

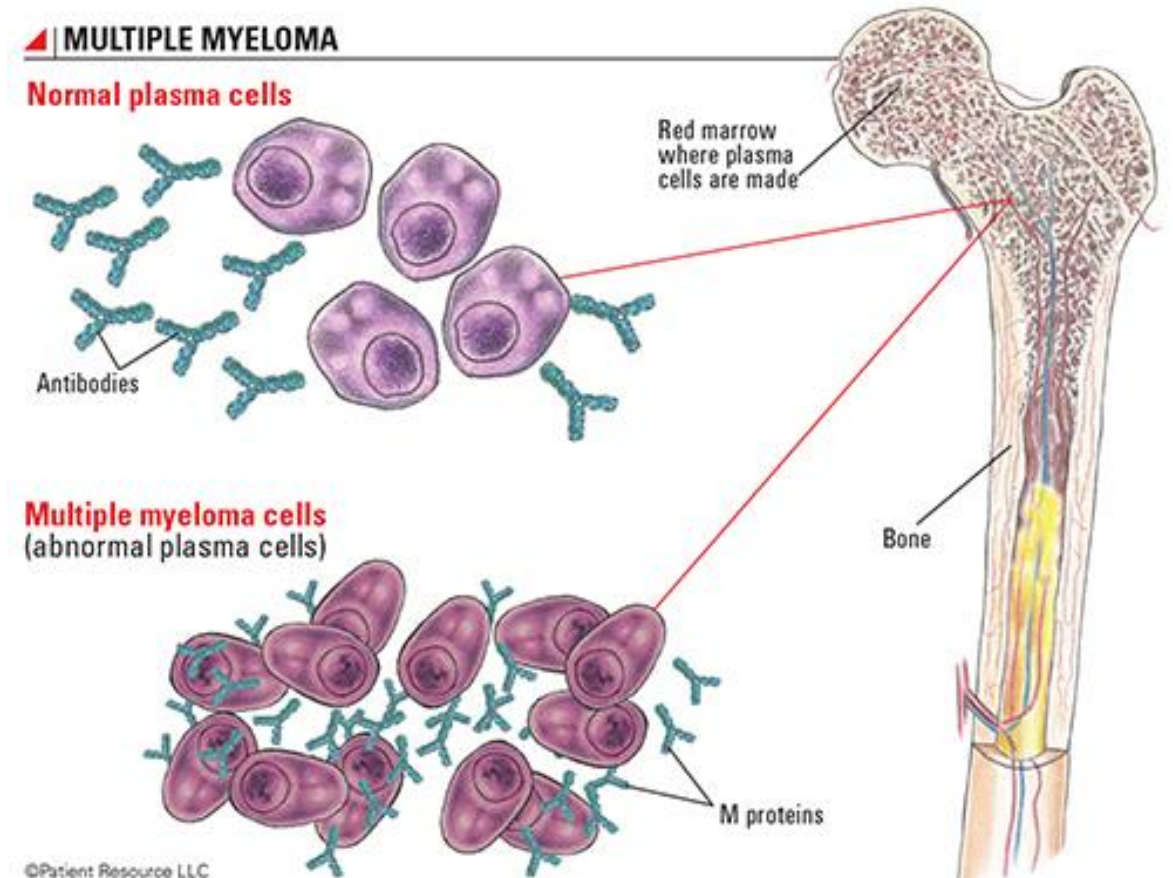
Background

Sponsor provides study data to Independent Review committee (IRC) or Independent Review Adjudication committee (IRAC) or Blinded Independent Central Review (BICR)
Vendors to support Clinical Trial endpoints.

- Data gets uploaded to separate Database
- IRC members provides MM response following IMWG-2016
- IRC is very costly (~ \$2M or more for a phase 3 study)
- IRC is time-consuming (operational management, development of charter and data transfer specifications, etc.).
- Delayed availability of IRC data (usually 6-8 weeks turn-around time)

Multiple Myeloma

- Cancer of plasma cells, i.e., excessive numbers of abnormal plasma cells in bone marrow
- Among hematologic malignancies, multiple myeloma is the second most prevalent blood cancer after non-Hodgkin lymphoma, representing 10% of hematologic malignancies



Objectives and Values

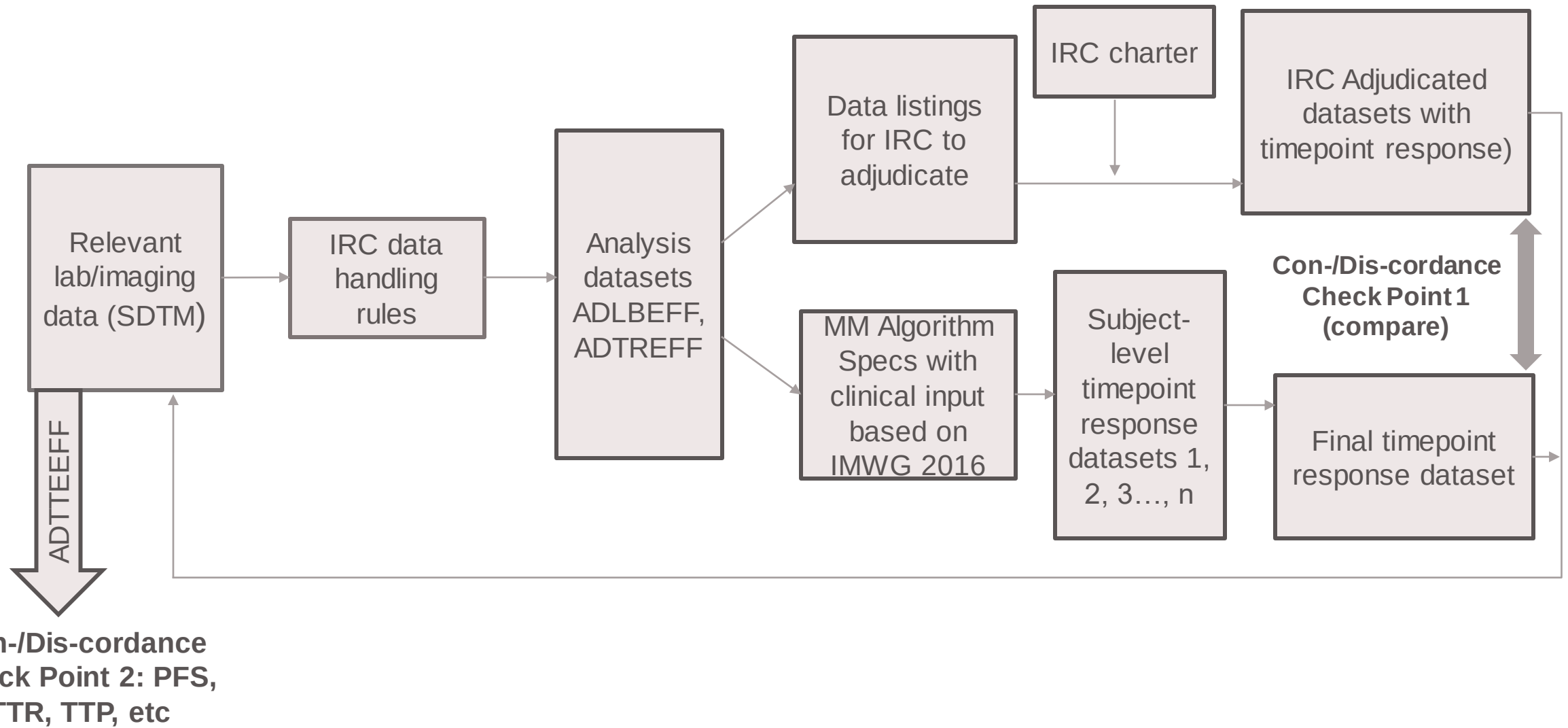
Objective:

Develop computerized algorithm for Multiple Myeloma studies using International Myeloma Working Group (IMWG-2016) Response Criteria to replace Independent Review committee (IRC).

Values:

- Reduce turn-around time
- Reduce cost
- Monitor cumulative number of PFS events real time and predict timing for analyses.
- Data review for response analysis

Overview of the Algorithm



Analysis Dataset Development

- Lab Efficacy analysis dataset (ADLBEFF)
 - ADaM BDS Structure
 - Lab parameters included
 - Implemented IRC data handling rules
- Plasmacytoma analysis dataset
 - ADaM BDS Structure
 - Includes Measurable, New lesion, Non-Measurable data and Bone Lesion information

Lab Data Points Per IMWG-2016

- Serum M-protein by electrophoresis (SPEP)
- Urine M-protein by electrophoresis (UPEP)
- Serum Immunofixation values
- Urine Immunofixation values
- Serum Free Light Chain values → Kappa, Lambda**
- Plasma cell % (Bone Marrow Aspirate)
- Plasma cell % (Bone Marrow Biopsy)

**Kappa Lambda ratio, Kappa Lambda Difference derived

Imaging Data Points Per IMWG-2016

- Bone lesion data
 - Increase in number of lesions from baseline
 - Increase in size of the lesion from baseline
- Measurable Plasmacytomas data
 - Total area
 - Percent change from BL in total area,
 - Percent change from Nadir in total area
 - ≥ 50 percent increase in the longest diameter of a previous lesion which is >1 cm in short axis
- Non-Measurable Plasmacytomas data → Absent, Present

Restructuring Data

- Requires one observation per subjects per visit / date
 - Merged 2 analysis dataset to one observation per subject per date/visit for each parameter
 - Imputation performed for Bone Marrow Biopsy if required
 - Local lab values needs to be considered if Central lab data is missing
 - Unscheduled data points requires consideration
- Plasmacytoma –Measurable, Non-measurable imputations

Baseline Categorization

➤ Baseline measurability Status

- Determined using Serum M-Protein, Urine M-Protein and Serum Free Light
- Plasmacytoma measurable and non-measurable baseline values
- Requires lab values to align with Protocol inclusion criteria

IMWG 2016 Response Derivation

- Response derived for each subject by visit / date
- Hierarchy - PD, sCR, CR, VGPR, PR, MR, SD
- Confirmatory response is derived
- Final response result mapped to SDTM.RS

IMWG 2016 Responses:

- Stringent Complete Response (sCR)
- Complete Response (CR)
- Very Good Partial Response (VGPR)
- Partial Response (PR)
- Minimal Response (MR)
- Stable Disease (SD)
- Progressive Disease(SD)

Validation and Concordance Checks

- Validated retrospectively using multiple studies.
- Performed concordance checks for
 - Best Overall Response
 - Response Date
 - PD / No PD assessment

Implementation Challenges

- Handling outliers
- Ensuring the discordance is not a programming error
- Understanding the algorithm from Clinical perspective
- Data Collection

Conclusion

- Successfully implement IMWG-2016 response criteria programmatically
- Availability of efficacy data in a shorter duration
- Supports monitoring cumulative PFS counts
- Followed CDISC data standards and ensure traceability
- Regulatory submission readiness and easy implementation

Useful Links

- [IMWG 2016](#) Response
- [Myeloma foundation IMWG](#)

Questions!



Thank you

If you have any questions, please contact

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