Gemeinsamer Bundesausschuss

Justification

on the Resolution of the Federal Joint Committee (G-BA) on the Finding in the Procedure of Routine Practice Data Collection and Evaluations according to Section 35a, paragraph 3b SGB V:
Risdiplam (spinal muscular atrophy) – Submission of study protocol and statistical analysis plan

of 4 April 2024

Contents

1. Legal basis

According to Section 35a, paragraph 3b, sentence 1 SGB V, the Federal Joint Committee (G-BA) can demand the pharmaceutical company to submit routine practice data collections and evaluations for the purpose of the benefit assessment within a reasonable period of time for the following medicinal products:

1. in the case of medicinal products authorised to be placed on the market in accordance with the procedure laid down in Article 14, paragraph 8 of Regulation (EC) No. 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1), as last amended by Regulation 162 Rules of Procedure last revised: 16 December 2020 (EU) 2019/5 (OJ L 4, 7.1.2019, p. 24), or for which a marketing authorisation has been granted in accordance with Article 14-a of Regulation (EC) No. 726/2004; and
2. for medicinal products approved for the treatment of rare diseases under Regulation No. 141/2000.

According to Section 35a, paragraph 3b, sentence 10 SGB V in conjunction with Chapter 5 Section 60 Rules of Procedure of the G-BA (VerfO), the G-BA reviews the data obtained and the obligation to collect data at regular intervals, at least every eighteen months.

2. Key points of the resolution

At its session on 21 July 2022, the G-BA decided on the requirement of routine data collection and evaluations for the active ingredient risdiplam in accordance with Section 35a, paragraph 3b, sentence 1 SGB V.

In order to check whether the G-BA's requirements for routine practice data collection and evaluations have been implemented, the pharmaceutical company submitted drafts for a study protocol and a statistical analysis plan (SAP) to the G-BA in due time in a letter dated 15 August 2023. The documents were reviewed by the G-BA with the involvement of the Institute for Quality and Efficiency in Health Care (IQWiG).

By letter dated 5 September 2023, the pharmaceutical company informed the G-BA that the orphan designation for Evrysdi (risdiplam) had been returned. By resolution of 21 July 2022, the G-BA justified the necessity for routine practice data collection and evaluations in accordance with Section 35a, paragraph 3b, sentence 1 SGB V for the active ingredient risdiplam by stating that, in particular, comparator data on treatment with risdiplam compared to existing appropriate therapeutic alternatives was identified as a relevant evidence gap for the early benefit assessment. Since the return of the orphan designation has no impact on the evidence gap identified and is therefore not associated with an improvement in the low evidence base for the assessment of the additional benefit, the routine practice data collection for the active ingredient risdiplam will be continued.

Based on the review of the documents, the G-BA came to the conclusion that the requirements for routine practice data collection and evaluations in the study protocol and SAP prepared by the pharmaceutical company and submitted to the G-BA for review were insufficiently implemented.

The present declaratory resolution and the associated justification establish and justify the necessary need for adaptation of the study protocol (version 1.0 (original); 31 July 2023) and the statistical analysis plan (version 1.0 (original); 10 August 2023).

2.1 Necessary adjustments to study protocol and statistical analysis plan

On the necessary adjustments in detail:

1. Question according to PICO: Patient population

   According to the resolution on requirements of 21 July 2022, the RPDC for risdiplam is to be carried out, taking into account data collected in parallel over time and data not collected in parallel over time, provided that these also meet the aforementioned data quality requirements. The pharmaceutical company only partially takes this into account in the inclusion and exclusion criteria, as in particular no limitations were made with regard to the criteria required to take into account data not collected in parallel. The inclusion and exclusion criteria should therefore be supplemented by the data quality requirements specified in the G-BA resolution.

   As an inclusion criterion, the pharmaceutical company specifies that the visit, which is defined as a baseline visit, must be between 6 weeks before and 3 weeks after the first application of the SMA medication. This inclusion criterion should be deleted as the procedure is inappropriate in terms of content (*see Section 17, Study design*: *Index date*).

   With regard to the exclusion criterion "Prior treatment of patients with risdiplam, nusinersen or onasemnogene abeparvovec before inclusion in the registry", it must be ensured that patients who have only received prior treatment with risdiplam or nusinersen in the form of bridging therapy are not excluded also per se. In order to achieve a sufficiently high sample size, it should be checked in these cases whether corresponding baseline data are available in sufficient quality at the time of the start of treatment or can be collected retrospectively in order to be able to enrol these patients in the RPDC study.

2. Question according to PICO: Outcome

   For a number of endpoints, the pharmaceutical company plans to carry out evaluations at several points in time (e.g. 12, 24 and 36 months after the start of treatment). In these situations, the evaluation that takes into account the longest possible observation period should always be presented as the primary analysis.

   An overview of the planned data collections is not included in the study documents. It is therefore not clear how often the individual data collection time points should be carried

out and whether, in particular, all motor endpoints are collected at every visit. A data collection plan must be added to provide an overview of the planned data collection time points during the course of the observation.

3. Question according to PICO: Outcome, morbidity

   The large number of endpoints describing motor function is problematic for the assessment of additional benefit. The pharmaceutical company should select pre-specified relevant endpoints and hierarchise the endpoints to reduce this multiplicity.

   According to the resolution of 21 July 2022, the motor function is to be performed using age-appropriate instruments. The pharmaceutical company plans to use several instruments for this purpose (Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders [CHOP-INTEND], Hammersmith Functional Motor Scale Expanded [HFMSE], Revised Upper Limb Module [RULM], 6-minute walk test and Bayley-III). Due to the exclusively population-dependent categorisation chosen by the pharmaceutical company without further information on the age range of the patients in whom the instruments are to be collected, it is not clear how patients who have the corresponding SMA type but have not yet reached the age at which the use of the respective instruments is recommended will be dealt with. In patients with type 2 SMA, for example, both the HFMSE and the RULM are not yet recommended for the age of onset of the disease (between 6 and 15 months of life). As the baseline assessment is planned at the start of treatment, operationalisation via the changes compared to baseline in this population is inappropriate. The study protocol must specify and ensure that age-appropriate instruments are used to assess motor function, particularly for operationalisations in which changes from baseline are assessed.

4. Question according to PICO: Outcome, Bayley III

   In pre-symptomatic patients, motor function should be assessed exclusively using the Bayley III gross motor skills subscale. For the Bayley scale, the manual describes different types of evaluation (*scaled scores, composite scores, percentile ranks,* and *growth scores*). The score to be evaluated must be specified in the study documents.

   The pharmaceutical company plans to evaluate the change in the score compared to baseline at 12, 24 and 36 months. If the patients are primarily identified via neonatal screening and treated soon after birth, it can be assumed that the age of this population corresponds approximately to the time after the start of treatment. However, the time of evaluation must be determined for all operationalisations depending on the time since the start of treatment.

5. Question according to PICO: Outcome, CHOP-INTEND

   The pharmaceutical company plans evaluations of the percentage of patients with type 1 SMA with a score of ≥ 40 on the CHOP-INTEND at the age of 12 months. However, there is no information in the study documents as to whether a score of 40 is a suitable response threshold. This is therefore to be supplemented. In addition, an evaluation only at the age

of 12 months with a total duration of observation of 36 months does not appear meaningful. The selected operationalisation must therefore ensure that the entire observation period is covered.

6. Question according to PICO: Outcome, 6-minute walk

   In addition to the HFMSE and the RULM, the pharmaceutical company plans to measure the 6-minute walking distance in patients with type 3 SMA. The selected operationalisations also include an improvement or deterioration in the distance walked by > 30 m 12, 24 and 36 months after the start of therapy. A justification as to why a change of > 30 m was selected as the response threshold has not yet been provided. The pharmaceutical company must therefore demonstrate that the selected response threshold (improvement or deterioration in the distance walked by > 30 m) is a clinically relevant change, otherwise continuous analyses must be defined.

   It is also questionable whether data collections at month 12 and possibly 24 after the start of treatment can be meaningfully interpreted for these patients. If the endpoint is to be used for the benefit assessment, an evaluation of the walking distance at month 36 after the start of treatment should therefore be defined without taking the baseline values into account.

7. Question according to PICO: Outcome, achievement of motor milestones

   The pharmaceutical company plans to collect a selection of 2 of the WHO motor milestones ("sit unassisted" and "walking without support"). There is no justification in the documents for not taking the "standing without support" milestone into account. An endpoint for the preservation of motor function is also not collected. The endpoint "standing without support" and an endpoint for maintenance of motor function should be added.

   The pharmaceutical company plans to operationalise the percentage of patients who reach the milestone at an age-appropriate point in time so that only the result of the first visit within a time window, by which healthy children usually reach this milestone (sitting: 9.5 to 13.5 months; walking: 18 to 22 months), is used. Patients who have not reached (or have already lost) the milestone at this visit are categorised as non-responders. This operationalisation only takes into account a small section of the entire duration of observation and is inappropriate.

   To operationalise the endpoint, time-to-event analyses or analyses of the percentage of patients who have reached a motor milestone at a point in time to be defined (e.g. 12 months, 24 months and 36 months after the start of treatment) are to be carried out.

8. Question according to PICO: Outcome, bulbar function

   Language skill is to be assessed using the expressive and receptive language subscales of the Bayley III at an age of 12, 24 and 36 months. As an operationalisation, the pharmaceutical company plans to assess the percentage of patients who show age-appropriate scores, defined as age equivalents, in the expressive language and receptive

language subscales. The Bayley III Manual mentions as a limitation of the age equivalents that they do not represent evenly distributed intervals within a scale and therefore small changes in the raw values can lead to large changes in the equivalents. The operationalisation must therefore be adjusted, e.g. as a change compared to baseline.

9. Question according to PICO: Outcome, further complications of the disease

   Based on the information provided in the study documents, the assessment of pain or fatigue appears to be based on a query only, without a specific instrument being used to assess these endpoints. However, this is not a valid data collection; age-appropriate, valid instruments should be used to assess the symptoms of pain or fatigue, if these are present. A corresponding review must be carried out.

   Orthopaedic complications are assessed via a composite endpoint of severe scoliosis (Cobb angle ≥ 40 degrees) and orthopaedic surgery. The pharmaceutical company does not justify why it restricts scoliosis only to severe events. A justification must therefore be added.

10. Question according to PICO: Outcome, adverse events (AEs)

    The pharmaceutical company plans time-to-event analyses for all AE endpoints - with the exception of the unplanned hospitalisations endpoint. However, if the duration of observation is comparable, evaluations of the percentage of patients with an event in the AE endpoints are preferable and should be performed for the RPDC study.

    Based on the documentation fields selected by the pharmaceutical company in SAP, the operationalisation of the planned endpoint "number of unplanned hospitalisations" is congruent with the operationalisation of "AEs leading to hospitalisation". The endpoint "number of unplanned hospitalisations" is therefore dispensable and should be deleted.

11. Question according to PICO: Outcome, serious adverse events (SAEs)

    There is no description of the operationalisation of the SAEs in the study documents, so this needs to be added. It should be made clear that an approximation of AEs that lead to hospitalisation or a prolongation of hospitalisation or AEs that lead to death is selected as operationalisation. The corresponding documentation fields in the SMArtCARE registry must be completed.

12. Data source/ study design: General

    Although the registry protocol for the SMArtCARE registry was available for review of the study documents, no coding manual or overview of the current data set was available. For the endpoints, some inclusion criteria and the confounders, the pharmaceutical company provides tabular information on the respective documentation fields in the registry in the study protocol and SAP. For an adequate assessment of the documentation of the relevant data, all relevant data fields with the corresponding operationalisation in the registry must be specified in the study documents. In addition, the current version of the coding manual must be submitted for supplementary information.

13. Data source: Inclusion of further registries

    The pharmaceutical company describes in the protocol that it may wish to include further registries, but does not provide any further details. Before the RPDC is launched, however, all registries used as data sources must be finalised and adapted to the RPDC requirements. If other registries are to be included, the inclusion of the respective registries must therefore be specified in advance and the suitability of the respective registries must be examined in accordance with the criteria specified by the G-BA in the resolution on requirements.

14. Data source: Confounder

    With regard to the identification of confounders, the pharmaceutical company refers, among other things, to the results of the systematic literature research in the study protocol for the routine practice data collection of onasemnogene abeparvovec. This is basically appropriate, but in the present procedure, patients with type 3 SMA are also part of the research question. Since it cannot be ruled out that other relevant confounders need to be considered for patients with type 3 SMA, a systematic literature research is required to identify any further potential confounders. With regard to the confounders selected by the pharmaceutical company, it is also necessary to describe how these are included in the model for the propensity score (PS) calculation (e.g. continuous or dichotomous) and what influence the classification into "less important" and "very important" has on the modelling of the PS.

15. Data source: Reporting dates

    There is no information in the study documents on how often the report is made to the SMArtCARE registry. The documentation of the collected data should be standardised for all patients directly after the respective visit in order to avoid reporting delays. In any case, the reporting dates in the selected data source must ensure that the data from the routine practice data collection are available for timely submission of the interim analyses specified in the resolution of 21 July 2022 and of the dossier for the new benefit assessment. This requirement must be saved in the study documents.

16. Data source: Completeness of the data

    To ensure the quality and completeness of the data collection, plausibility checks are carried out in accordance with the information in the study documents. These need to be specified in the study protocol.

    According to the information in the resolution on requirements of 21 July 2022, the pharmaceutical company describes that source data verification should be carried out for 100% of patients per data collection site for the primary endpoint and for at least 10% of randomly selected patients per data collection site for all other endpoints over the period since the start of data collection. Information on the consequences of the planned Source Data Verification (SDV) should be added.

17. Study design: Index date

The pharmaceutical company describes the visit between 6 weeks before and 3 weeks after the first application of the SMA medication as the index date, i.e. the date for the start of the observation. This approach is inappropriate. It is not adequate to record the index date before the start of treatment for some patients and after the start of treatment for others. The day of the treatment decision should be used as the index date in accordance with the procedure for target trial emulation, or the best possible approximation should be made. The index date should therefore be defined as the date of the treatment decision (or a best possible approximation). A possible bridging therapy is to be considered as part of the therapy concept and must therefore be covered by the observation period.

18. Study design: Assignment to the treatment groups

    Based on the information in the study documents, treatment of patients who have received bridging therapy (e.g. until gene therapy is used) remains unclear. Since a corresponding bridging therapy is not designed for further treatment, it should be noted that patients who have received a bridging therapy are assigned to the subsequent therapy.

19. Study design: Sample size planning

    The sample size planning for patients with SMA type 2 and type 3 based on the RULM must be adjusted, as the operationalisation of the RULM is inappropriate (*see Section 3, Question according to PICO*: *Outcome, morbidity*)

    For patients with type 1 SMA, sample size planning should be based on the composite endpoint of death or prolonged ventilation, operationalised over the time until the event. The assumed event percentage of 22% for the comparator arm and the expected effect magnitudes on which the sample size planning is based are incomprehensible. For patients with type 1 and type 2 SMA, the assumptions for the effect magnitude are also close to the shifted null hypothesis formulated by the pharmaceutical company. This procedure inevitably leads to very large sample sizes. The assumptions for the presented sample size planning for patients with SMA type 1 and the assumptions for the effect magnitude for patients with SMA type 1 and type 2 should therefore be justified in more detail and adjusted if necessary.

    If disproportionately high sample sizes result for the initially selected endpoint despite a review of the underlying assumptions, the pharmaceutical company must examine or carry out further possible sample size planning on the basis of other benefit endpoints and, if necessary, also on the basis of harm endpoints.

    Due to the high level of uncertainty in estimating an adequate sample size in this procedure, the study documents must also include a review of the assumptions made during the course of data collection.

    The distribution ratios of the treatment arms on which the respective sample size planning is based must be added.

20. Study design: Discontinuation criteria

    The study documents contain information on the discontinuation criterion, but it remains unclear how to proceed for the populations for which no sample size planning has yet been carried out. This must be completed by the pharmaceutical company. It should also be added to the study protocol that any decision to discontinue the RPDC (and to change the sample size estimate) will be made in consultation with the G-BA.

21. Study design: Duration of observation

    The pharmaceutical company does not state the length of follow-up of the patients in the study documents. According to the information in the resolution on requirements of 21 July 2022, all patients in the RPDC study must be followed up for at least 36 months, regardless of any change in treatment.

    For the endpoint "unplanned hospitalisations", the pharmaceutical company only plans to include events before the change of treatment in the analysis and to end the follow-up "for these patients" with the change of treatment. It remains unclear to which patients this statement refers. For the endpoint "unplanned hospitalisations", the fact that the follow-up ends with the change of treatment should be deleted.

22. Study design: Information on the data collection process

    If possible, descriptive analyses of data on prospectively enrolled patients should also be submitted for the required information on the course of data collection 6 months after the start of the study.

23. Data evaluation: Estimand

    The pharmaceutical company determines two different estimands depending on the primary endpoint. An estimand based on the treatment policy strategy and an estimand using a hypothetical strategy for the primary endpoint "unplanned hospitalisations" to address change of treatment in pre-symptomatic patients.

    It should be noted in the study documents that the primary estimand of the RPDC study corresponds to the treatment policy strategy and includes the evaluation according to the intention-to-treat (ITT) principle for all patient-relevant endpoints (*for the evaluation of adverse events, see also section 29*). In both treatment arms, data collections and events under possible subsequent therapies are also taken into account.

24. Data evaluation: Responder analyses

    The pharmaceutical company states that it wants to specify three effect measures for responder analyses: attributable risk, odds ratio and relative risk. Information on the planned test statistics for the planned responder analyses and the model to be used for the calculation is missing and must therefore be added.

25. Data evaluation: continuous evaluations

For continuous evaluations, according to information in the study documents, a mixed model for repeated measures (MMRM) with the covariates treatment, visit, interaction between treatment and visit, adjusted for the value at the start of study, should be used and Cohen's d and 95% confidence interval should be used as the effect measure. The missing information on the effect measure and the test statistics must be added.

Cohen's d should also be used as an effect measure for the continuous evaluations of the 6MWT endpoint. The use of Cohen's d is inappropriate in this case as the results of this endpoint are based on a natural scale. The study documents must therefore specify that the relevance of the results is interpreted on the basis of the scale of the instrument (i.e. in this case, on the basis of the distance walked).

26. Data evaluation: Sensitivity analyses

    According to the information in the study documents, analyses are selected as sensitivity analyses in which observations after any change in treatment are not included in the analysis. In addition, due to possible heterogeneity between the two therapy options in the comparator arm, heterogeneity analyses should be performed in the data evaluation. These are to be added to the study documents.

27. Data evaluation: Subgroup analyses

    The pharmaceutical company plans to conduct subgroup analyses for various characteristics. The choice of potential effect modifiers largely corresponds to those that will also be analysed in the routine practice data collection of onasemnogene abeparvovec. In the present procedure, however, the age at enrolment in the study (pre-symptomatic, type 2 SMA and type 3 SMA) or the age at diagnosis (type 3 SMA) are to be analysed as subgroup features instead of the age at the start of treatment. This should be standardised and extended to all populations under investigation. In principle, meaningful separation values should be selected, which may differ between the individual populations to be analysed. The planned categorisation of the subgroups on the basis of the median must therefore be justified. Information on the planned methodology for the subgroup analyses and on how to interpret the results has not yet been provided and needs to be supplemented.

28. Data evaluation: Propensity score method

    When dealing with extreme weights when using the Inverse Probability of Treatment Weighting (IPTW) procedure, the pharmaceutical company plans to replace propensity scores that are below 0.05 or above 0.95 with the corresponding threshold value. The planned procedure must be substantiated with suitable literature. In the absence of relevant literature, the procedure must be adapted, e.g. by truncating extreme weights.

    A detailed description of the testing of the analysis population and target population according to PS weighting is missing in the documents submitted and must be supplemented by the pharmaceutical company.

29. Data evaluation: adverse events (AEs)

The pharmaceutical company describes that the AE endpoints are to be analysed using a hypothetical strategy. For this purpose, patients in both treatment arms are censored at the time of the change in treatment.

It should be noted in the study documents that, in addition to the planned evaluation using a hypothetical strategy, evaluations using a treatment policy strategy will also be conducted for the AE endpoints.

30. Data evaluation: Dealing with missing values

    If the month is missing in the case of missing dates, the pharmaceutical company plans to use the date on which the patient was last considered event-free. However, the planned replacement of the month for patients with an event potentially leads to bias and is inappropriate. This provision should therefore be deleted. Instead, the pharmaceutical company shall add what efforts are being made to minimise the rate of missing values in the date specification.

    The pharmaceutical company plans not to impute missing values and not to use a variable as a confounder if more than 40% of the data for the respective variable is missing. However, the resulting consequences for the evaluations and interpretation of the data have not yet been presented and discussed.

31. Data evaluation: Missing information

    The pharmaceutical company must provide the following missing information in accordance with the resolution on requirements of 21 July 2022:

    - Dealing with implausible data and outliers
    - Information to check the extent to which the data on nusinersen and onasemnogene abeparvovec collected in parallel, as well as data not collected in parallel, are suitable for pooled analysis,
    - Information to check the extent to which any data comparing risdiplam versus nusinersen and onasemnogene abeparvovec from different data sources are suitable for a pooled analysis

In order to avoid inconsistencies, the pharmaceutical company must check whether the need for changes in the study protocol described here leads to corresponding subsequent changes in the SAP and vice versa.

In addition to the mandatory adaptations, the G-BA makes the following recommendations for further adaptations of the study protocol and the SAP:

1. Question according to PICO: Outcome (general)

    In order to ensure the comparability of the results between the routine practice data collection in spinal muscular atrophy, a standardised approach is preferable. It is therefore recommended to select operationalisations for identical endpoints that are as uniform as

possible and that have been assessed as appropriate in the procedure for routine practice data collection of the active ingredient onasemnogene abeparvovec.

2. Question according to PICO: Outcome, morbidity

   A standardised procedure is also recommended for onasemnogene abeparvovec for the required selection and hierarchisation of relevant endpoints for the description of motor function.

3. Question according to PICO: Outcome, achievement of motor milestones

   With regard to the required addition of an endpoint for the preservation of motor function, it is recommended that this be operationalised as "time from reaching a motor milestone to complete loss of this skill".

4. Question according to PICO: Outcome, Bayley III

   For pre-symptomatic patients, motor function has so far only been assessed using the Bayley III gross motor skills subscale. It is recommended to use CHOP-INTEND as an alternative or supplement, which is also suitable for the corresponding age group.

5. Data source: Outcome, morbidity (respiratory function)

   Permanent ventilation is operationalised here as ventilation for at least 16 hours a day for at least 21 consecutive days. There is no justification as to why the pharmaceutical company only assumes permanent ventilation after 21 consecutive days. It is therefore recommended to align the operationalisation of permanent ventilation with the operationalisation in the routine practice data collection of onasemnogene abeparvovec (2 consecutive documentations of ventilation for ≥ 16 hours/day).

6. Data source: Outcome, morbidity (bulbar function)

   Language skill is to be assessed using the expressive and receptive language subscales of the Bayley III in pre-symptomatic and patients with type 1 SMA. Since the assessment of the development of language skill also appears to make sense in patients with type 2 and type 3 SMA, a corresponding assessment is also recommended for these patient populations.

2.2 Deadline for submission of the revised study protocol and statistical analysis plan

The revised study protocol and the revised SAP are to be submitted to the G-BA by 2 May 2024.

When submitting the revised version of the SAP and the study protocol, the pharmaceutical company must ensure that the changes made can be completely and clearly understood. For this purpose, a version of the documents must usually be submitted in which the changes have been marked in detail, as well as a current version of the documents without marking the changes. Amendments that do not result from the need for adjustment set out in this resolution and the justification shall be justified separately.

3. Process sequence

In order to check whether the requirements of the G-BA for routine data collection and evaluations for the active ingredient risdiplam have been implemented as specified in the resolution of 21 July 2022, the pharmaceutical company submitted drafts of a study protocol and a SAP to the G-BA. The documents were reviewed by the G-BA with the involvement of IQWiG.

The issue was discussed in the working group WG RPDC and in the Subcommittee on Medicinal Products.

At its session on 4 April 2024, the plenum decided on the result of the review regarding the submitted study protocol (version 1.0 (original); 31 July 2023) and the statistical analysis plan (version 1.0 (original); 10 August 2023).

Chronological course of consultation

Session	Date	Subject of consultation
WG RPDC	16 October 2023 5 January 2024 15 January 2024	Consultation on the study protocol and statistical analysis plan (SAP)
Subcommittee Medicinal products	23 January 2024	Consultation on the result of the review of the study protocol and SAP
Plenum	4 April 2024	Resolution on the result of the review of the study protocol and SAP

Berlin, 4 April 2024

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken