Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Gold R, et al. Incidence and mitigation of gastrointestinal events in patients with relapsing-remitting Multiple Sclerosis receiving delayed-release dimethyl fumarate – a German phase IV study (TOLERATE). Ther. Adv. Neurol. Dis.; 2018… (TBD)

Supplementary Appendix

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1. Scales for grading Gastrointestinal (GI) outcomes and severity (MOGISS; MAGISS)

Two scales for the description of the gastrointestinal status were handed to the patients via an electronic device in order to document self reported outcomes of their GI status.

In an overall scale the patient was to document his overall GI status in the "Modified Overall Gastrointestinal Symptom Scale (MOGISS)". If the patient was ideed experiencing GI events he was additionally asked to specify these using the "Modified Acute Gastrointestinal Symptom Scale (MAGISS)". The two scales were implemented in a guided menue via an electronic self reporting device ("LogPad") which is described in this supplement under item 2.

Below please find the explanation for the two gastrointestinal scales (MOGISS; MAGISS) as is was pesented to the study patient. The version for this study was, of course, in german language.

1.1. Modified Overall Gastrointestinal Symptom Scale (MOGISS)

Instructions for Using the Modified Overall Gastrointestinal Symptom Scale (MOGISS).

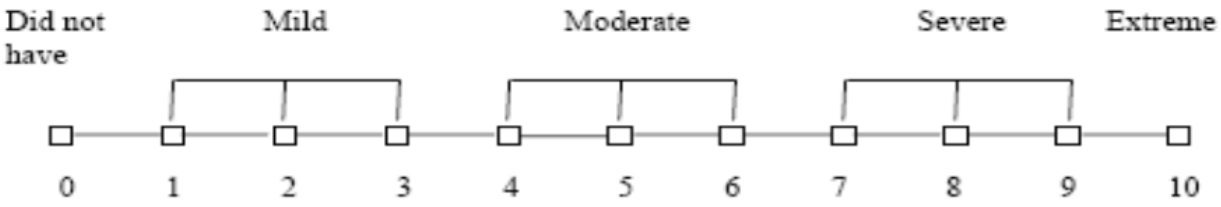
The MOGISS is about side effects related to your gastrointestinal (GI) system.

By GI system side effects, we mean nausea, diarrhea, upper abdominal pain, lower abdominal pain, vomiting, indigestion, constipation, bloating (abdominal distention), and flatulence (gas).

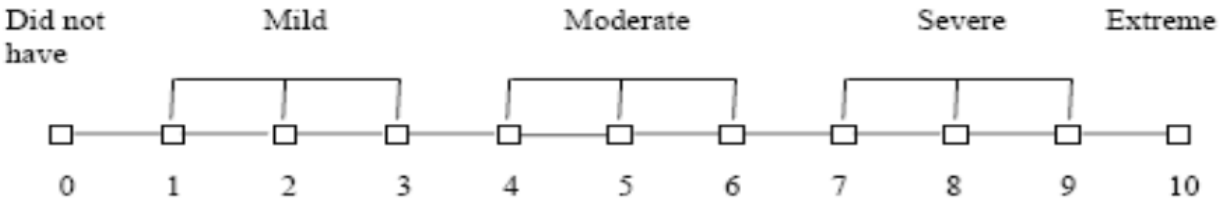
You may or may not have any of the side effects. If you have GI system side effects, you may have just one of them, or you may have two or more of them at once.

The following questions should be answered at the same time each day, before your morning drug administration.

1. OVERALL during the past 24 hours, how would you rate your GI side effects (nausea, diarrhea, upper abdominal pain, lower abdominal pain, vomiting, indigestion, constipation, bloating, and flatulence)?



2. OVERALL during the past 24 hours, how BOTHERSOME were your GI side effects (nausea, diarrhea, upper abdominal pain, lower abdominal pain, vomiting, indigestion, constipation, bloating, and flatulence)?



1.2. Modified Acute Gastrointestinal Symptom Scale (MAGISS)

Instructions for Using the Modified Acute Gastrointestinal Symptom Scale (MAGISS)

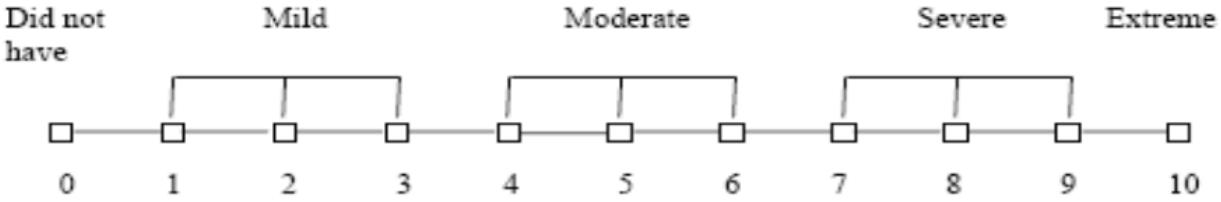
The questions in the MAGISS are about side effects of your gastrointestinal (GI) system following drug administration.

By GI system side effects, we mean nausea, diarrhea, upper abdominal pain, lower abdominal pain, vomiting, indigestion, constipation, bloating (abdominal distention), and flatulence.

If you have GI system side effects, you may have just one of them or you may have two or more of them at once. You may or may not have any of the side effects being asked about following administration of your study medication.

The following questions relate only to the period of time since you took the Tecfidera and should be completed within 10 hours of taking your Tecfidera (2 times/day).

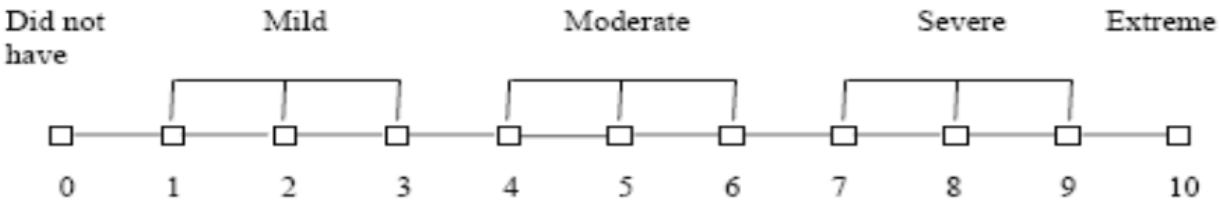
1. Please rate the intensity of your NAUSEA on the following scale by selecting one number.



If you did not have nausea, skip to number 4 below.

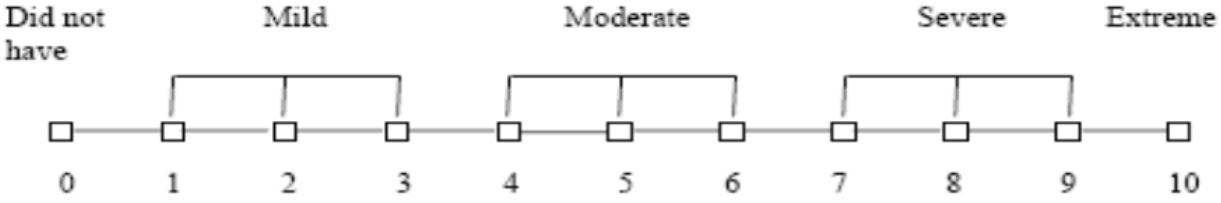
2. What time did your nausea start? _____
3. What time did your nausea end? _____

1. Please rate the intensity of your DIARRHEA on the following scale by selecting one number.



If you did not have diarrhea, skip to number 7 below.

2. What time did your diarrhea start? _____
3. What time did your diarrhea end? _____
4. Please rate the intensity of your UPPER ABDOMINAL PAIN on the following scale by selecting one number.



If you did not have upper abdominal pain, skip to number 10 below.

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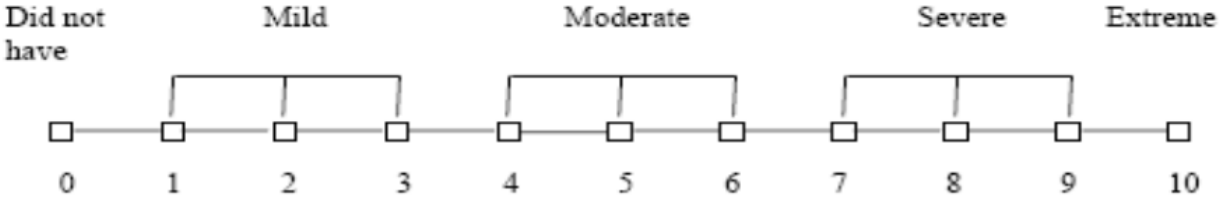
5. What time did your upper abdominal pain start? _____
6. What time did your upper abdominal pain end? _____
7. Please rate the intensity of your LOWER ABDOMINAL PAIN on the following scale by selecting one number.



If you did not have lower abdominal pain, skip to number 13 below.

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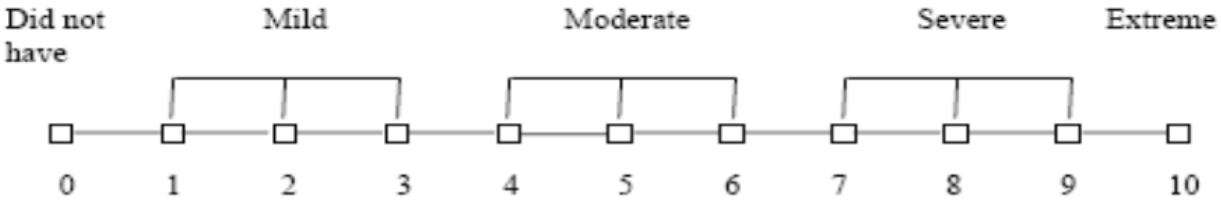
8. What time did your lower abdominal pain start? _____
9. What time did your lower abdominal pain end? _____
10. Please rate the intensity of your VOMITING on the following scale by selecting one number.

If you did not have vomiting, skip to number 16 below.

11. What time did your vomiting start? _____
12. What time did your vomiting end? _____
13. Please rate the intensity of your INDIGESTION on the following scale by selecting one number.



If you did not have indigestion, skip to number 19 below.

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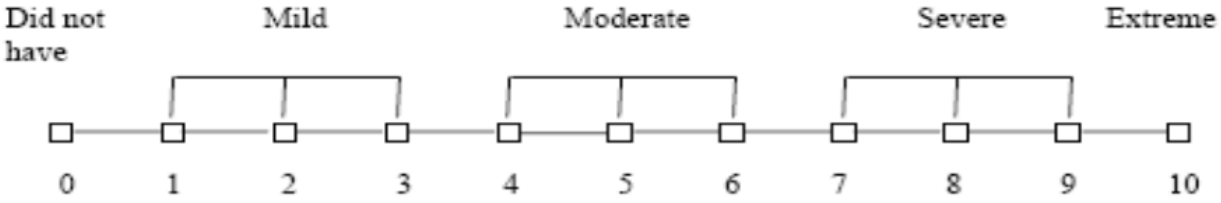
14. What time did your indigestion start? _____
15. What time did your indigestion end? _____
16. Please rate the intensity of your CONSTIPATION on the following scale by selecting one number.



If you did not have constipation, skip to number 22 below.

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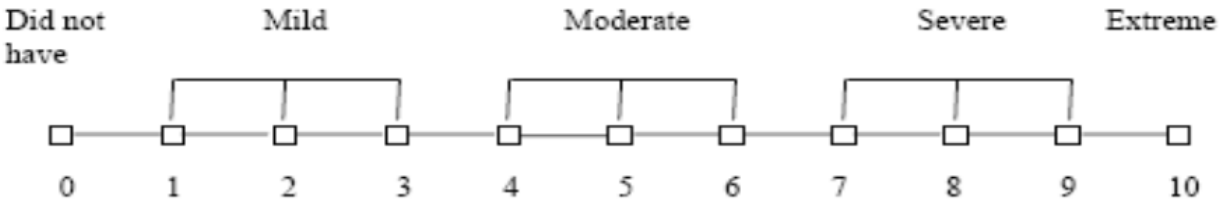
17. What time did your constipation start? _____
18. What time did your constipation end? _____
    Please rate the intensity of your BLOATING (ABDOMINAL DISTENTION) on the following scale by selecting one number.

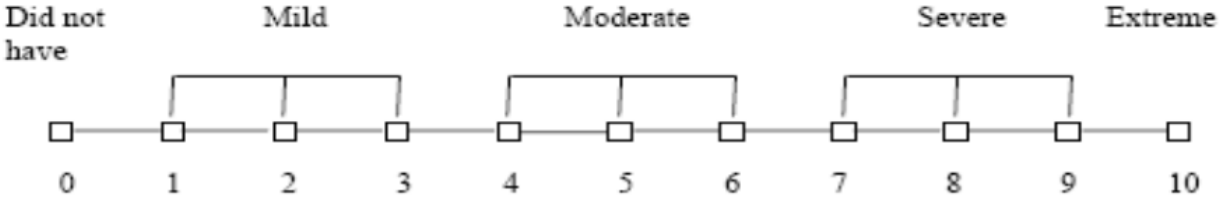


If you did not have bloating, skip to number 25 below.

19. What time did your bloating (abdominal distention) start? _____

20. What time did your bloating (abdominal distention) end? _____

21. Please rate the intensity of your FLATULENCE (GAS) on the following scale by selecting one number.



If you did not have flatulence, you have finished the questionnaire.

22. What time did your flatulence (gas) start? _____

23. What time did your flatulence (gas) end? _____

2. Reporting of Self reported outcomes via “LogPad”

Self reported Outcomes (SRO) were documented directly by the patient by an electronic device (“LogPad”; Fig 1). By using this device the patient was instructed to submit GI side effects directly in the device in a guided menue for the MOGISS and the MAGISS (Fig. 2) and for GI medication given in´a pick list and free text (Fig. 3.).

Fig. 1 Electronic Device for recording of GI side effects

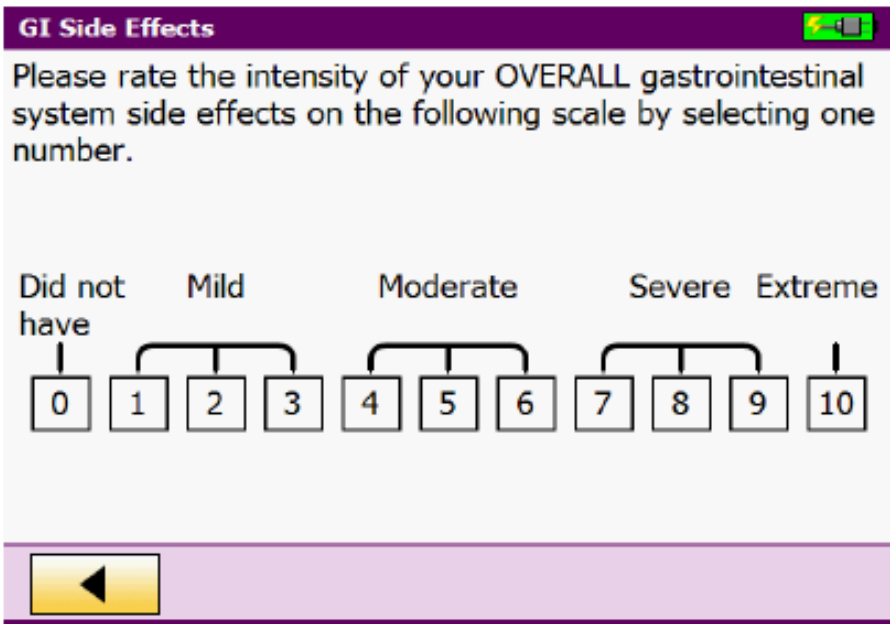


Fig. 2 MOGISS questionaire as presented on the “LogPad.

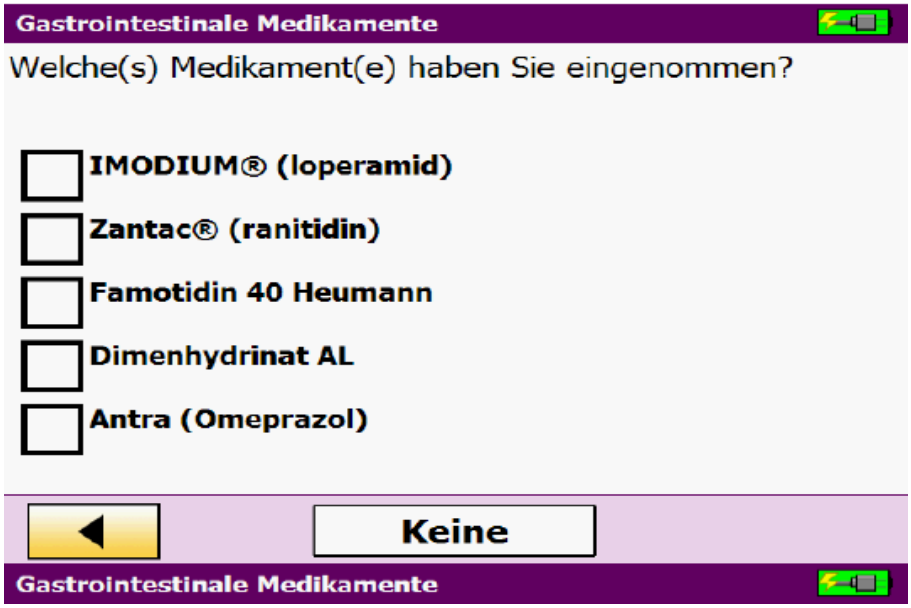


Fig.3 GI medication (extract) as presented on the “LogPad.