

Diagnostic study of HLA-DQ2 typing for gluten sensitivity in IBS patients

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Background

- HLA-DQ2 in predicting response to GFD in IBS-D patients*
 - Sensitivity: 92%
 - Specificity: 52%
- German guideline: GFD-attempt in IBS patients (preferentially IBS-D) is allowed

* Wahnschaffe et al. 2007

Questions to be answered...

Prospectively and double-blinded:

- Can HLA-DQ2 typing be used in non-constipated IBS patients (i.e. IBS-D or IBS-M) to identify gluten-sensitives?

Observational/non-controlled:

- What is the portion of GS in our population?
- What is a GFD-responder?
- How long do we need to treat with GFD to know?

Exclusion criteria

- <18 years old
- pregnant
- constipated IBS
- other medical conditions presenting with IBS-like symptoms identified by...
 - medical history
 - physical examination
 - blood tests (TSH, ESR and/or CRP, total IgA, anti-tissue-transglutaminase IgA, WBC, hemoglobin, platelets, creatinine, β hCG)
 - lower and/or upper GI-endoscopy
 - abdominal ultrasound
 - lactose intolerance test
 - stool examination on pancreatic elastase
 - stool culture
 - skin-test for wheat allergy
- chronic gastrointestinal or pancreatic diseases
- "alarm symptoms":
 - weight loss
 - fever

Inclusion criteria

- fulfill the Rome III criteria for
 - diarrhea-dominant IBS (IBS-D) or
 - mixed-type IBS (IBS-M)
 - based on diagnostic questionnaire *
- abdominal discomfort or pain...
 - for ≥ 2 days/week within the last three months (onset of symptoms at least 6 months prior to the diagnosis)
 - is associated with ≥ 2 out of 3 criteria
 1. improvement with defecation
 2. onset associated with a change in frequency of stool, and/or
 3. onset associated with a change in appearance of stool.

Endpoints in IBS

- SGA=subjective global assessment of relief^{1,2}:

Telephone call once a week

“Compared to the way you felt before you entered the study, were your IBS symptoms over the last seven days“:

- (1) completely relieved
- (2) considerably relieved
- (3) somewhat relieved
- (4) unchanged
- (5) worse

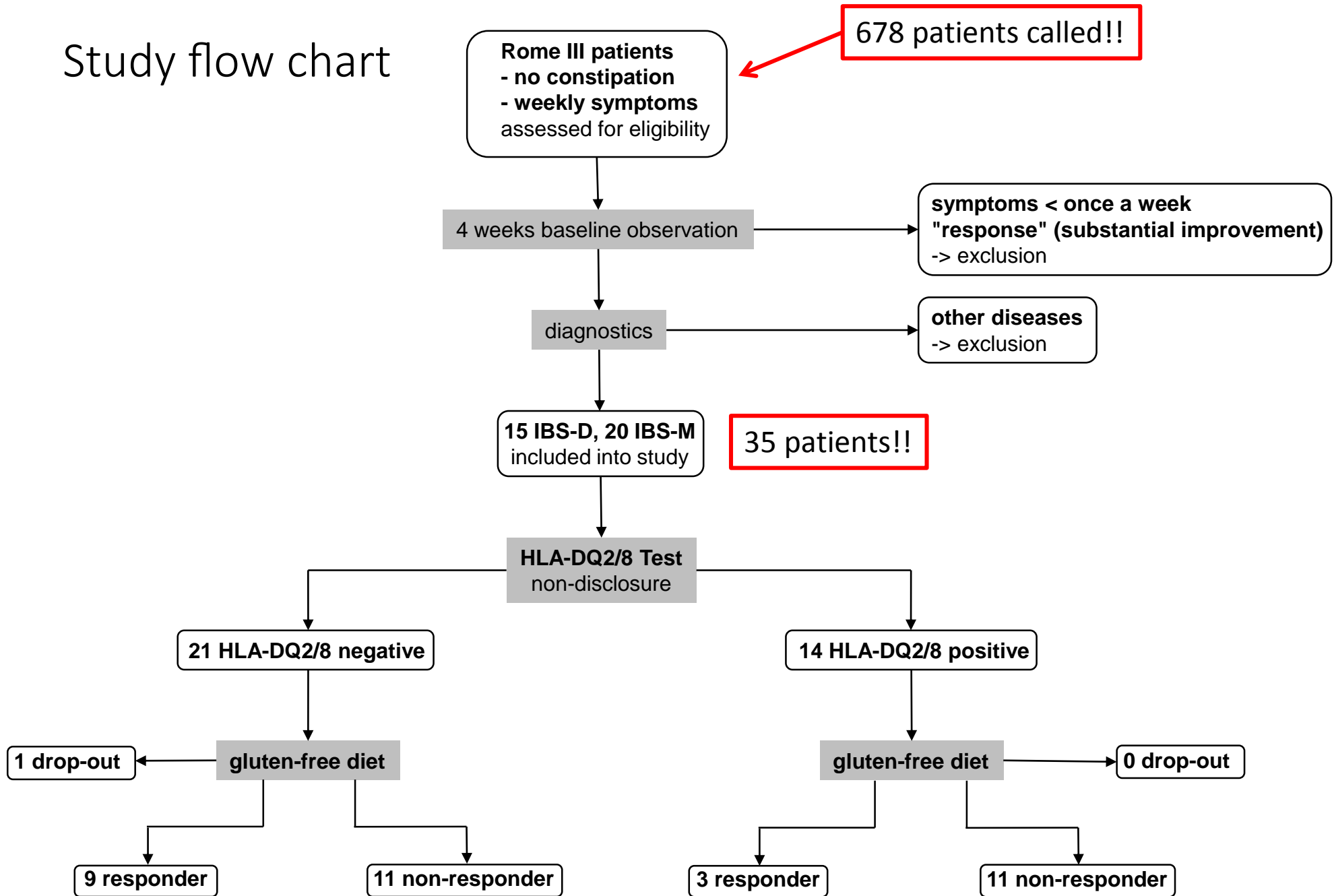
- Responders:

Patients who answered “considerably relieved” or “completely relieved” on at least 75% of weeks over the last four months of treatment

¹, Müller-Lissner et al., *Aliment Pharmacol Ther* 2001; Vol. 15:1655.

², Müller-Lissner et al., *J Clin Epidemiol* 2003; Vol. 56:310.

Study flow chart



Study population

	IBS-D	IBS-M	total
male	5 (33%)	4 (20%)	9 (26%)
female	10 (67%)	16 (80%)	26 (74%)
DQ2+	3 (20%)	7 (35%)	10 (29%)
DQ8+	1 (7%)	3 (15%)	4 (11%)
DQ2-DQ8-	11 (73%)	10 (50%)	21 (60%)
total	15	20	35

Results I

- Responders = gluten-sensitive
defined as patients who answered “considerably relieved” or “completely relieved” on at least 75% of weeks over the last four months of treatment
- 12 of 35 improved at least 75% of weeks
GS prevalence 34% (95% CI: 21-51%)

Responders by DQ2/8 and by IBS type

		Responders	total
HLA	DQ2+ or DQ8+	3 (21%)	14
	DQ2-DQ8-	9 (43%)	21
type	IBS-D	5 (33%)	15
	IBS-M	7 (35%)	20
total		12 (34%)	35

Summary I

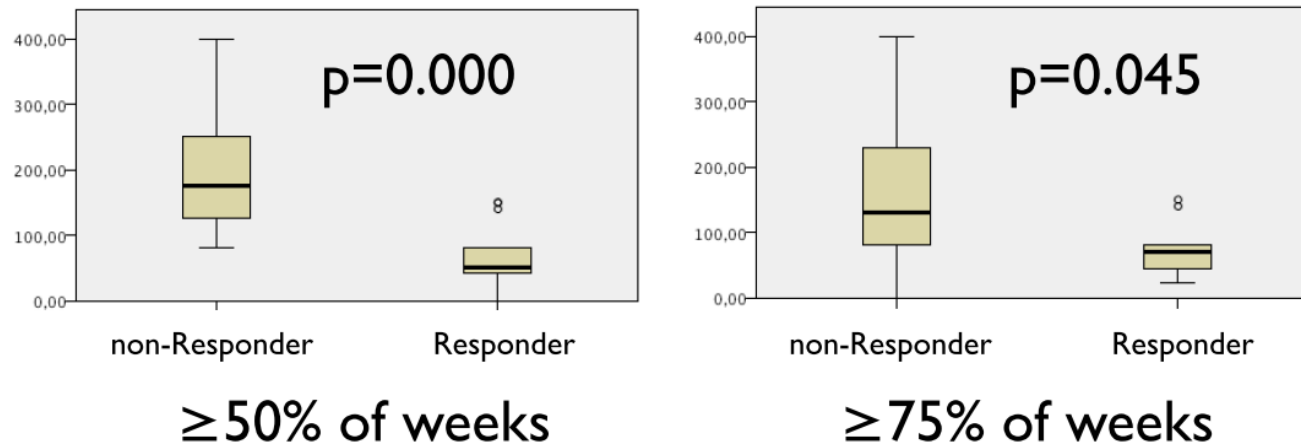
- 34% (95% CI: 21-51%) of patients with IBS-D or IBS-M were gluten sensitive.
- similar proportions in IBS-D and IBS-M patients.
- no correlation between GS and HLA-DQ2/8 status

Prevalence GS in this study

- $\geq 75\%$ of weeks improved: 34% (95% CI: 21-51%)
- $\geq 50\%$ of weeks improved: 51% (95% CI: 36-67%)

Definition of a GFD-responsive patient $\geq 50\%$ or $\geq 75\%$ of weeks improved?

- e.g. IBS Symptom Severity Score



- similar results in IBS-QOL and EQ-5D VAS

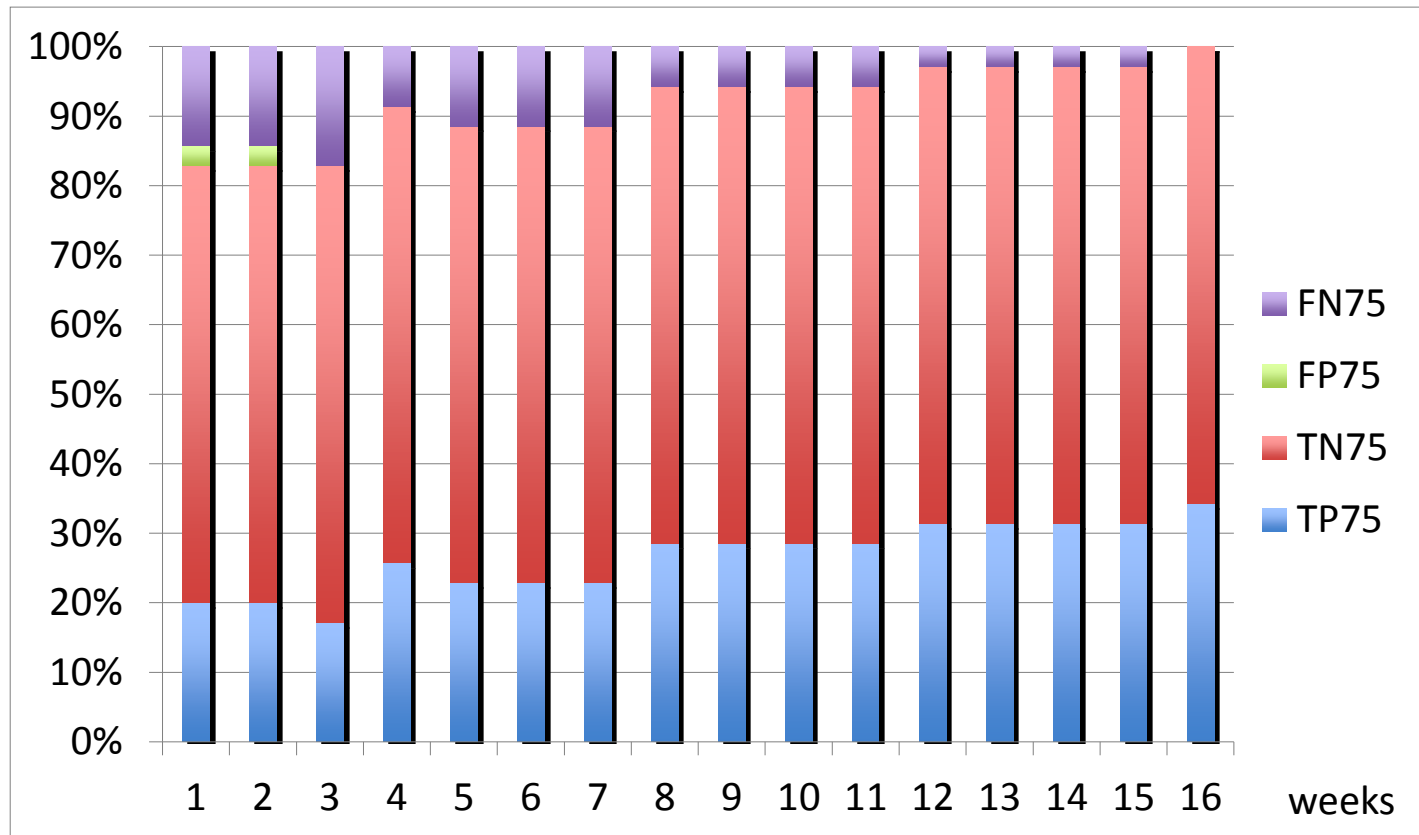
How long to observe?

→ performance over time

- 6 IBS-D and 7 IBS-M started to be “considerably relieved” or “completely relieved” only after 2 months of GFD
- then reached a stable plateau
- All 13 patients were classified as non-responders (by 75% criterion)
- 7 of these patients were even non-responders by 50% criterion

How long to observe?

→ performance over time



Responders $\geq 75\%$ of weeks

Definition of a GFD-responsive patient – partial responders?

- complete relief of symptoms after 16 weeks of GFD:
33% (4 of 12) responders
- 1-year follow-up (telephone call)....

1-year follow-up: Who remained on a GFD?

	Strict GFD	GFD with exceptions	No GFD	total
Responder	7 (64%)	4 (36%)	0 (0%)	11
Non-responder	6 (33%)	4 (22%)	8 (45%)	18

Included for follow-up: n=29 (of 35)

Summary II

- Differences in secondary outcomes between responders and non-responders were more clear-cut with a 50% response rate than with the 75% response rate.
- Early responses were mostly stable, i.e. there were few false positives.
- Delayed responses were common!
(2-month-GFD trial??)
- Complete responders were rare
- many non-responders stay on GFD because of “sub-optimal” improvement of symptoms.

Thanks!

Dr. Schär AG

- Jacqueline Pante

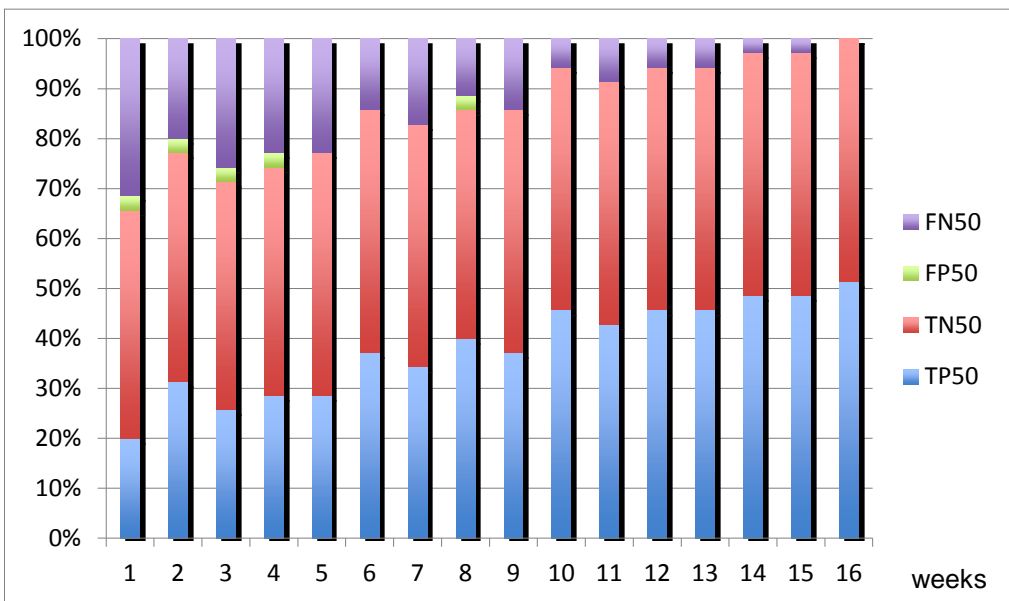
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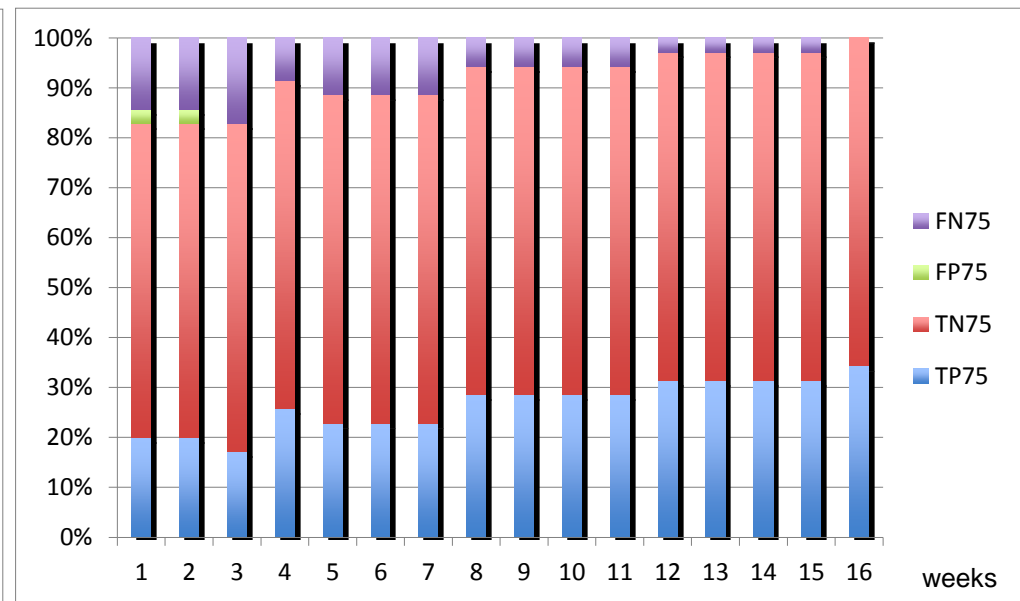


How long to observe?

→ performance over time



$\geq 50\%$ of weeks



$\geq 75\%$ of weeks

Study flow chart

