Genetic polymorphisms associated with sustained response to anti-TNF drugs in children with Inflammatory Bowel Disease

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Introduction

- One-third of the patients do not respond to anti-TNF therapy
- Genetic markers may predict individual response to this treatment
- Having biomarkers of response before starting therapy would allow us to choose the most appropriate therapy to start with.
- Currently we only have biomarkers of response once the therapy has started
- These treatments are administered equally to children and adults

… Can we treat children the way we treat adults?

In children, IBD has different and important connotations:

- Delayed growth
- Worse prognostic
- Early biological therapy
- Having to live much longer with a disease that has no cure

Objective

To identify biomarkers in children that predict response to anti-TNFs in short, medium and long-term, as well as those associated with drug levels in respondent patients

Material and methods

- 107
- 14 Spanish hospitals

-*TLR2 (rs1816702 y rs3804099)*

-*TLR4 (rs5030728)*

-*TLR9 (rs352139)*

-*LY96 (11465996)*

-*TNFRSF1A (rs4149570 y rs767455)*

-*TNFRSF1B (rs1061622 y rs1061624)*

-*TNFAIP3 (rs6927172)*

-*IL10 (rs1800872 y rs3024505)*

-*MAP3K14 (rs7222094)*

-*CD14 (rs2569190)*

-*TNF-α (rs1800629 y rs361525)*

-*IL6 (rs10499563)*

-*IL17A (rs2275913)*

-*IL1B (rs4848306)*

-*FCGR3A (rs396991)*

-*FASL (rs762000)*

12-months response (n=63)

*Logistic regression

24-months response (n=74)

*Kaplan-Meyer curves

Response until end of follow-up (n=74)

*Kaplan-Meyer curves

Treatment failure: Suspension of treatment due to relapse
Confused variables: Type of IBD y Treatment

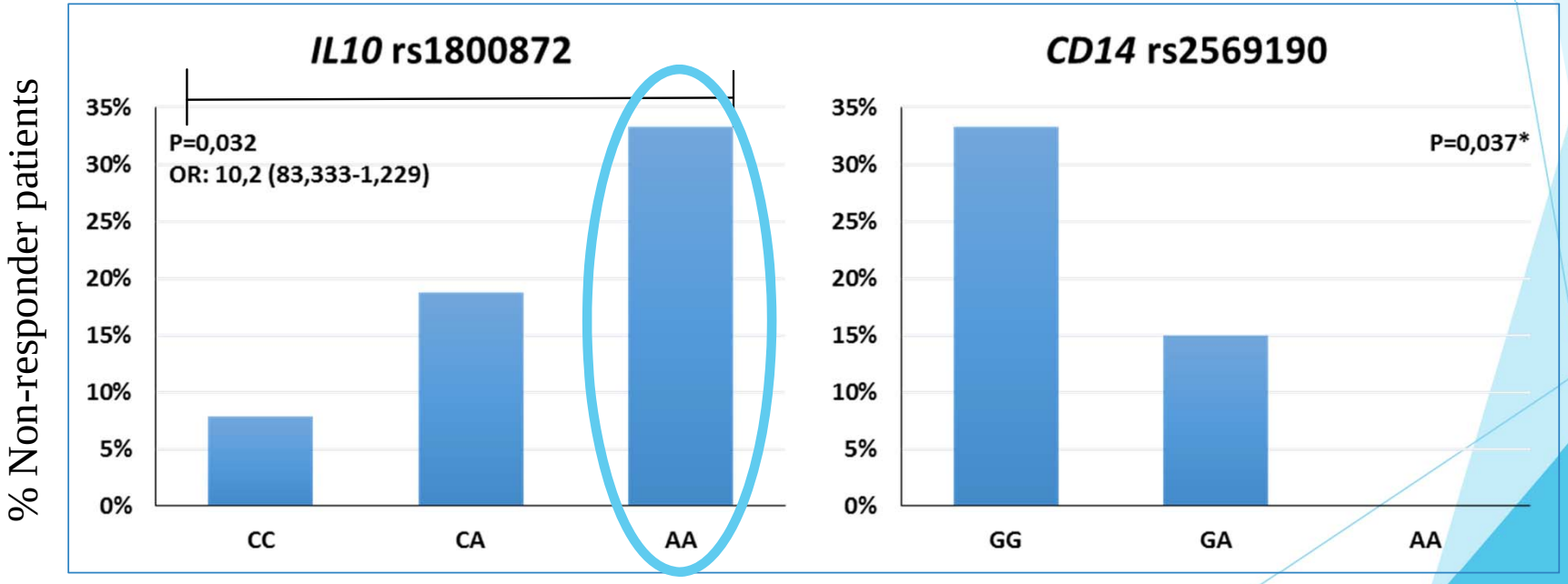
Drug levels (n=95)

*Logistic regression

Results

Association of genetic polymorphisms with response to anti-TNF therapy.

Polymorphisms associated with 12-months response to anti-TNFs

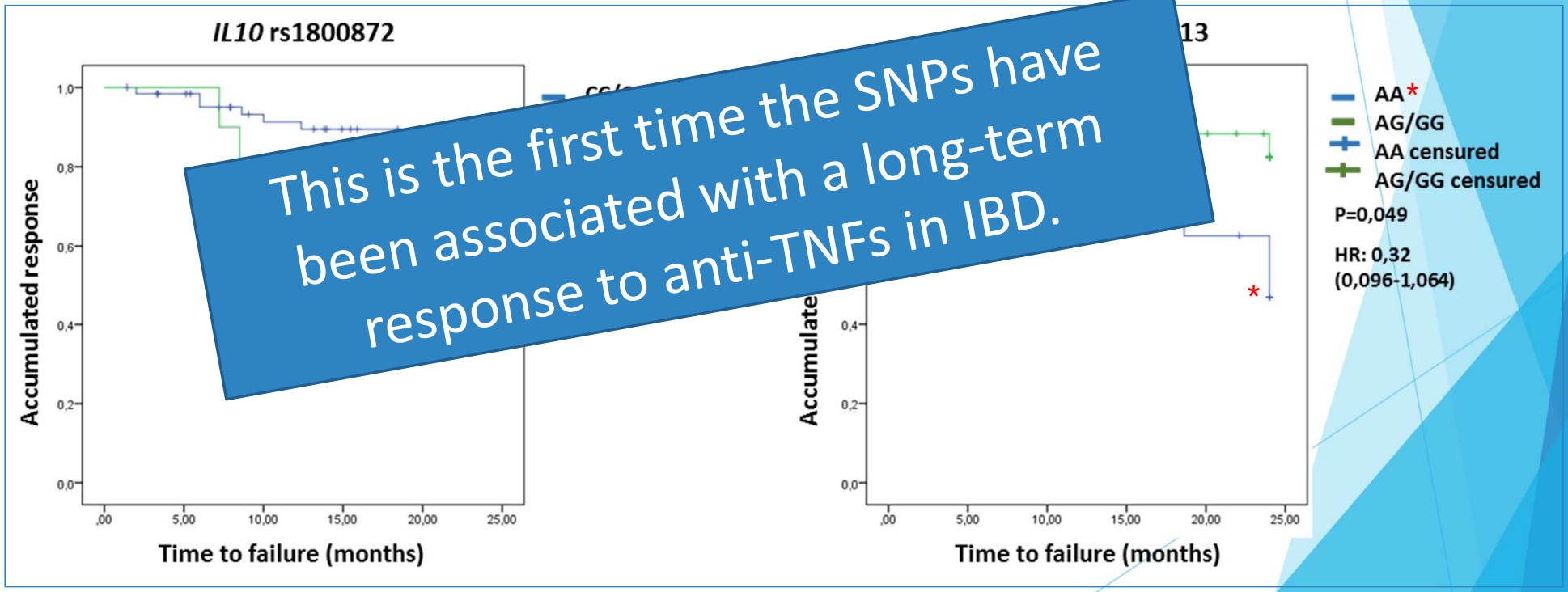


*P value of univariate analysis, OR not avaiable

Results

Association of genetic polymorphisms with response to anti-TNF therapy.

Polymorphisms associated with 24-months response to anti-TNFs

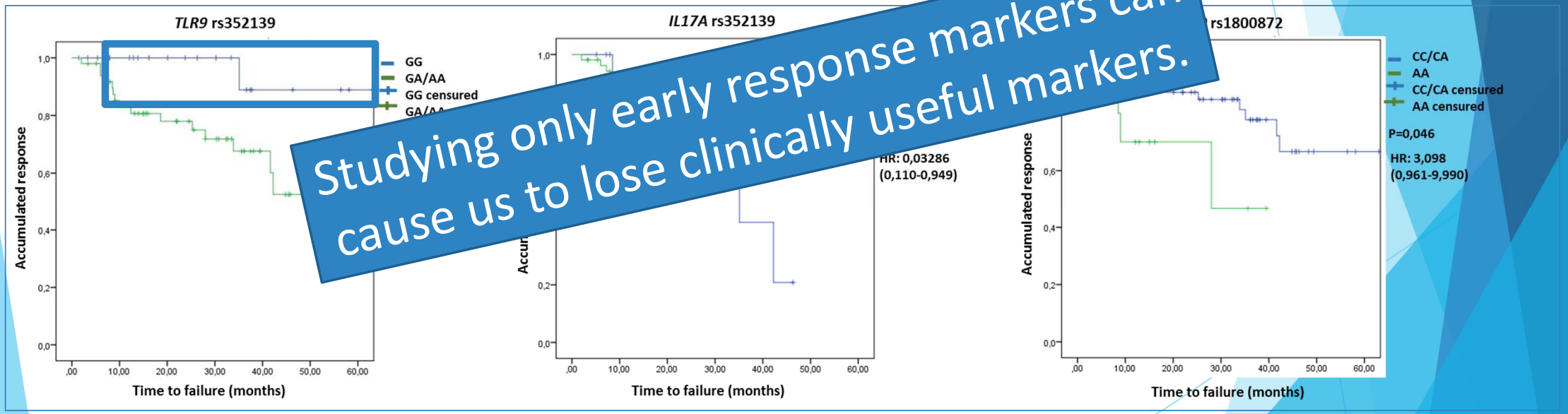


This is the first time the SNPs have been associated with a long-term response to anti-TNFs in IBD.

Results

Association of genetic polymorphisms with response to anti-TNF therapy.

Polymorphisms associated with sustained response to anti-TNF treatment

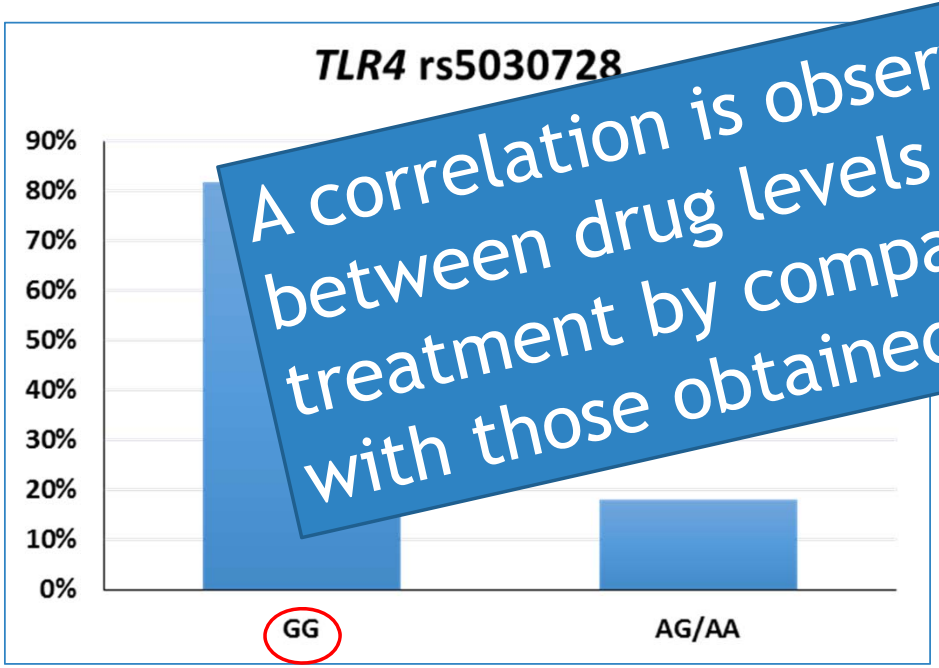


Studying only early response markers can cause us to lose clinically useful markers.

Results

Association of genetic polymorphisms with drug levels

Anti-TNF drug levels below the therapeutic range



Lack of response

A correlation is observed in this SNP between drug levels and response to treatment by comparing the results with those obtained in other studies.

CONCLUSIONS

- Markers of response to short, medium, and long-term anti-TNFs were first identified, as well as those associated with drug levels in children with IBD
- Genotyping of these genetic variants in the pediatric IBD population could be included in clinical guidelines to select the most appropriate therapeutic regimen for these patients.

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Thank you!

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