



INFLUENCE OF JAK1 GENE POLYMORPHISMS ON TREATMENT RESPONSE TO JAK INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS.

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INTRODUCTION

JAK inhibitors (JAKi) block the JAK-STAT pathway, crucial in immune cell regulation. Genetic variations in JAK1 may influence treatment outcomes in rheumatoid arthritis (RA), highlighting the importance of understanding individual genetic profiles to optimize therapeutic response to these drugs.

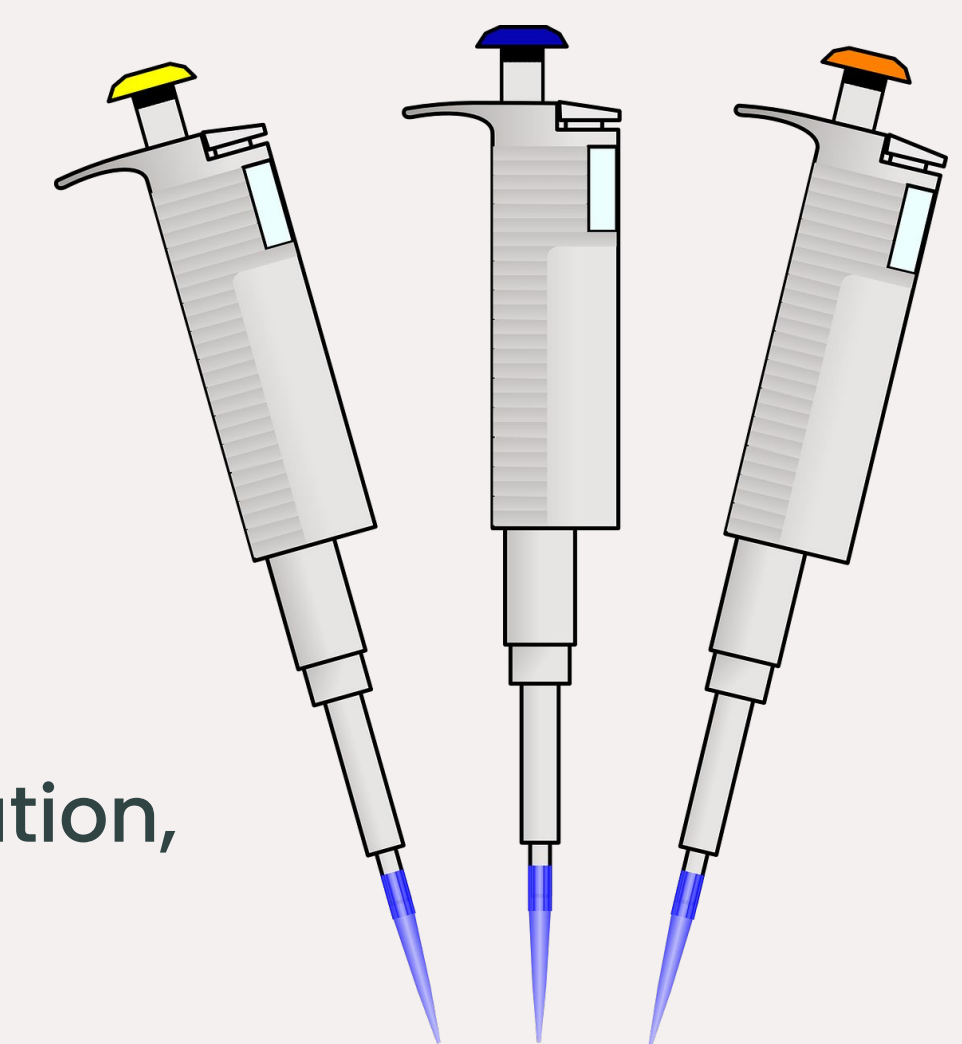


AIM

Evaluate the role of SNPs (**rs2230587**, **rs310241**, **rs2230588**) in JAK1 on response to JAK inhibitors (**upadacitinib**, **baricitinib**, **tofacitinib**, and **filgotinib**) in RA patients.

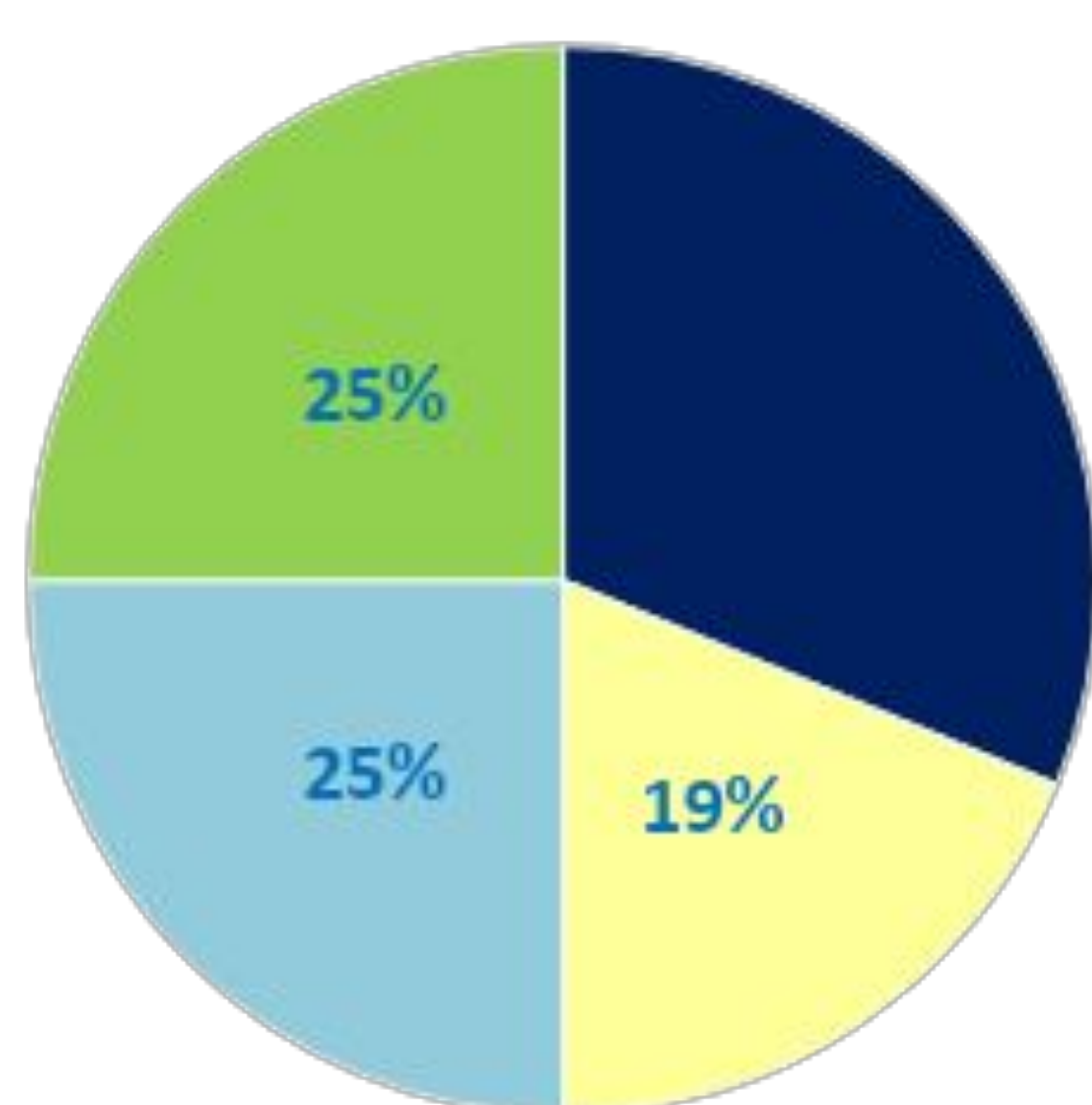
METHODOLOGY

- **Study Design:** Ambispective observational cohort study of 41 RA patients.
- **Data Collection:** Electronic prescriptions and medical records; genotyping via Taqman PCR Real-Time.
- **Variables:**
 - **Quantitative:** Age, Body mass index (BMI), disease duration, previous biologic therapies, treatment duration, Disease Activity measures (DAS28) at 0, 3, 6, 12 months.
 - **Qualitative:** Sex, first JAKi used, treatment discontinuation, dose changes.
- **Analysis:** R Commander.



RESULTS

REASONS FOR DISCONTINUATION



- Secondary failure
- Primary failure
- Adverse events
- Lack of response

PATIENT CHARACTERISTICS

- 41 patients analyzed: 32 women
- Median age: 53.5 years (47.7-60.5)
- Median BMI: 27.6 (24.4-33.3)
- Median disease duration: 11 years (6.7-20)
- Prior biologic therapies: 2 (1-3.2)
- Median treatment duration: 21 months (13-40)

KEY GENOTYPE ASSOCIATIONS WITH TREATMENT RESPONSE.

- rs2230587-AG genotype: Higher EULAR response (p=0.032, OR=12).
- rs2230588-CC genotype: Enhanced response (p=0.022, OR=9).
- rs310241-GG genotype: Associated with remission (p=0.036, OR=1.85).

TREATMENT DETAILS

- JAKi distribution
 - tofacitinib (14/41)
 - baricitinib (12/41)
 - upadacitinib (10/41)
 - filgotinib (5/41).
- Treatment discontinuations: 16 patients.
- Dose adjustments: 6 patients.

CONCLUSION

EULAR response to JAKi drugs was associated with different SNPs of the JAK1 gene. Nonetheless, further studies with large cohorts have to be performed to confirm these data in order to apply personalized medicine in clinical practice routine.