

# **PRAME mRNA Expression in AML/MDS and HLA Genotype Analysis: Impact on Population Coverage and Design of TCR-Based Immunotherapies**

---

**Richard Addo MD, PhD**

**62<sup>nd</sup> ASH Annual Meeting**

**Dec 5-8 2020**

**Disclosure:** employee of Medigene Immunotherapies GmbH

# Introduction

- Study objectives
  - To determine how many and which HLA-A-restricted TCRs are needed to ensure optimal coverage of the Caucasian population
  - To determine PRAME expression in AML/MDS patients
- PRAME as a target for TCR-T immunotherapies
  - A well described cancer-testis antigen
  - Highly expressed in tumors but scarce or absent in normal tissues
  - Highly expressed in most solid and liquid cancers, including AML/MDS
  - PRAME can stimulate cytotoxic lymphocytes

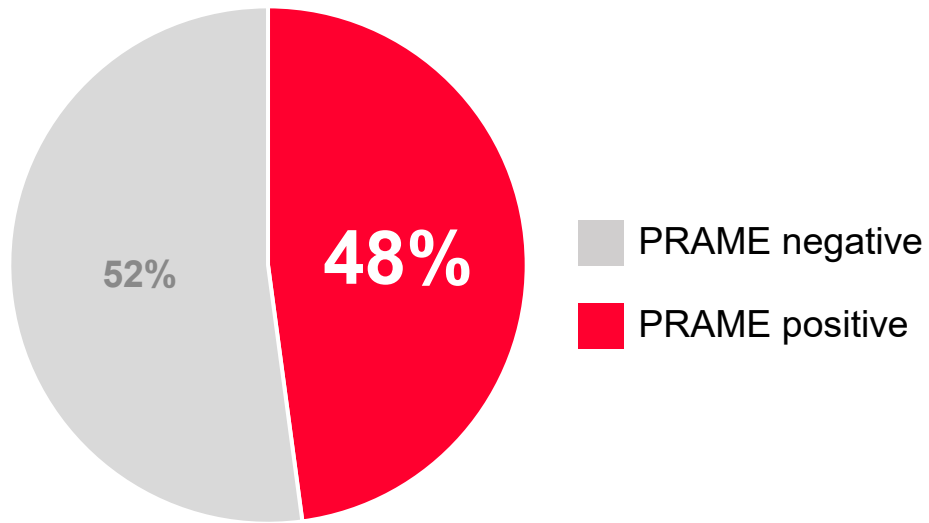
# Overview of samples analysed in the study

<b>AML/MDS patient cohort (N=165)</b>		
<b>Parameter</b>		<b>Outcome, n (%)</b>
<b>Disease indication</b>	AML	<b>133 (80.6%)</b>
	MDS	<b>32 (19.4%)</b>
<b>Disease status</b>	First time (initial) diagnosis	<b>96 (58.2%)</b>
	Relapsed Refractory	<b>68 (41.2%)</b>
	Unknown	<b>1 (0.6%)</b>
<b>Samples</b>	Paired BM and PB	<b>111 (67.3%)</b>
	Unpaired/Only PB	<b>54 (32.7%)</b>
<b>HLA-A distribution analysis (N=141)</b>		
<b>Healthy donors</b>	PB	<b>141 (100.0%)</b>

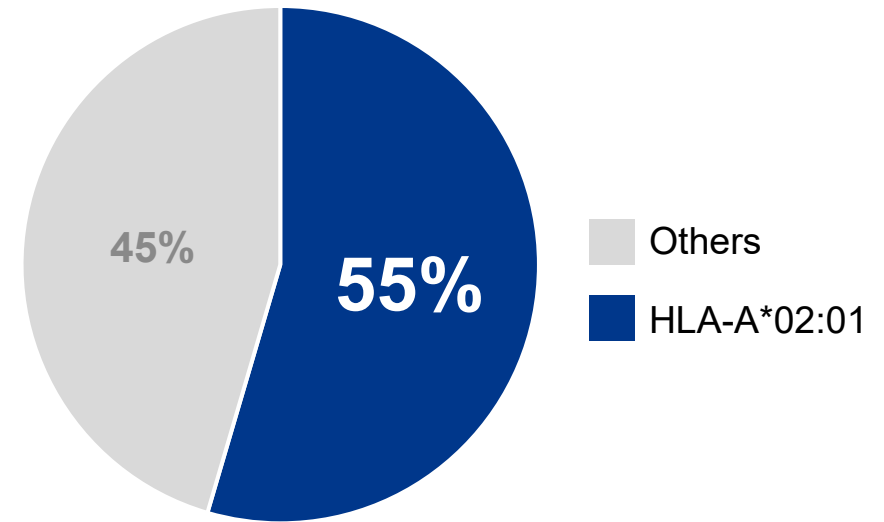
# Methods

- PRAME measurement
  - via qRT-PCR of cDNA transcribed mRNA isolated from peripheral blood (PB) or bone marrow aspiration (BM)
  - positivity threshold of 99 PRAME mRNA copies at 100% assay specificity was determined using samples from healthy donors
- HLA genotyping was performed using next generation sequencing

# PRAME expression and HLA-A\*02:01 in AML/MDS patients

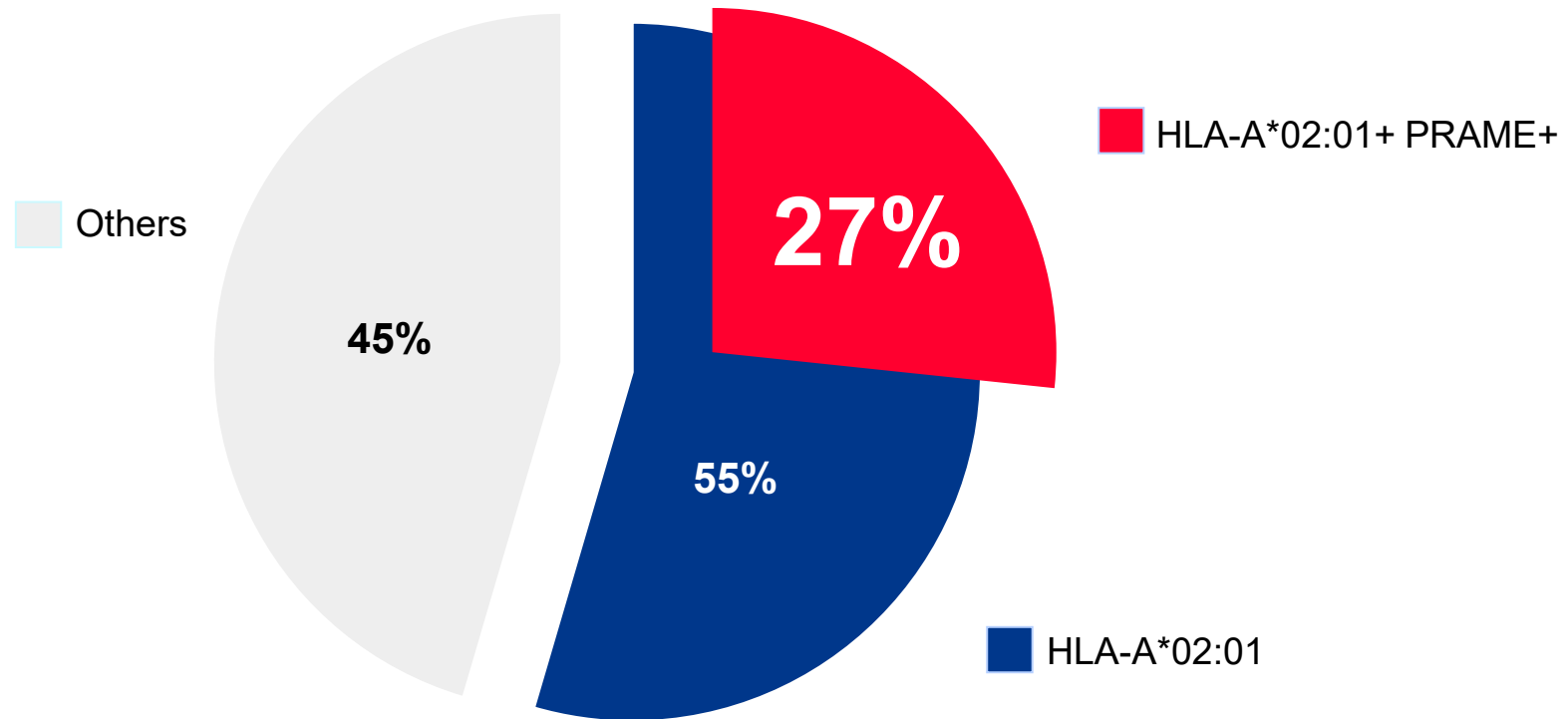


- 48% of all patients (N= 165) were PRAME positive
- Considered positive if expression in PB or BM was  $\geq 99$  copies

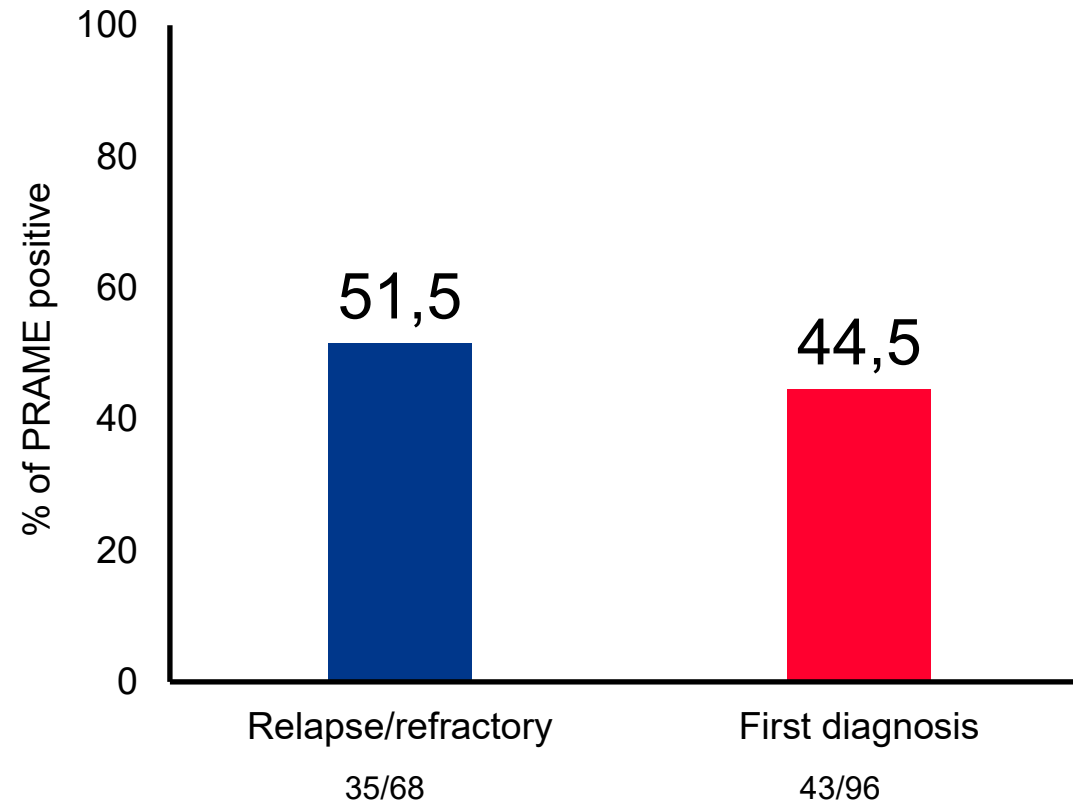


- 55% of all patients (N= 165) were HLA-A\*02:01 positive, Distribution could be skewed due to inclusion of allo-HSCT patients with already known HLA-A\*02:01

# 'Double' positivity of AML/ MDS patients



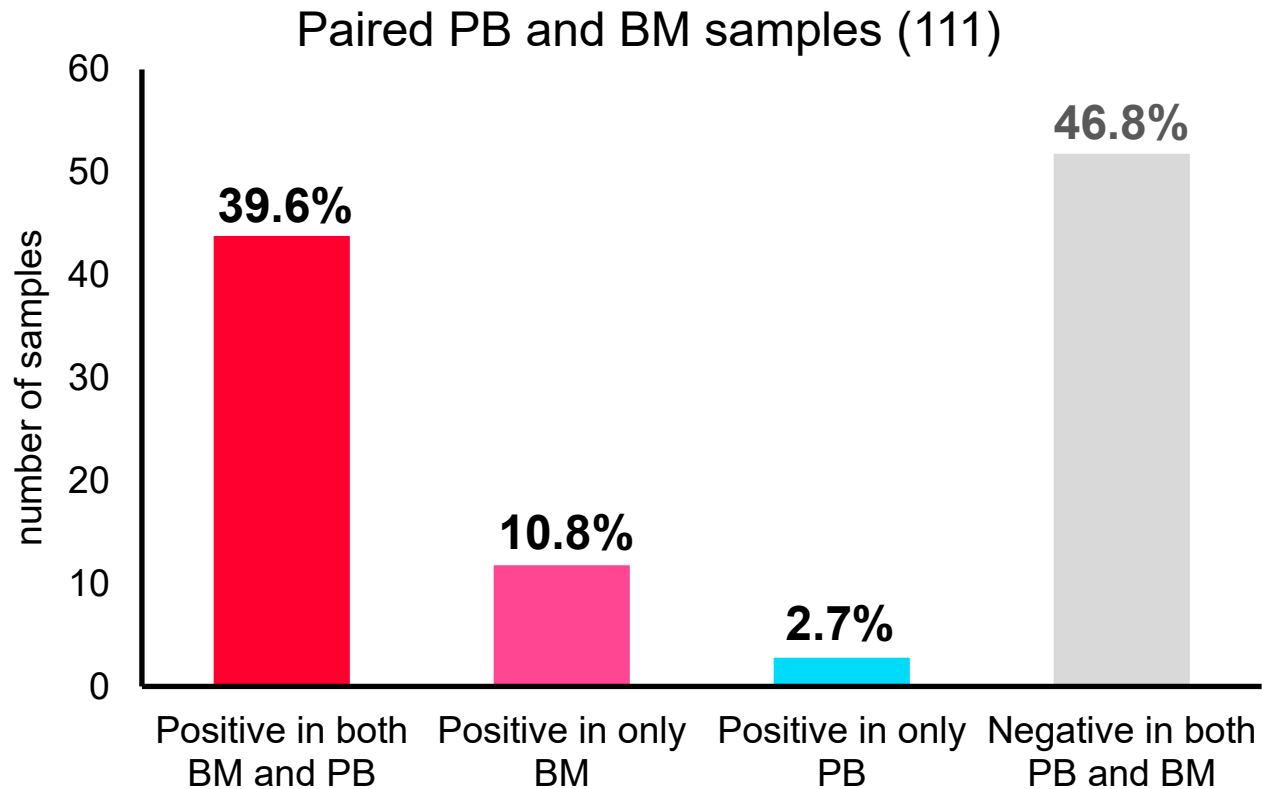
# PRAME expression is similar between first diagnosis and relapsed/refractory AML/MDS patients





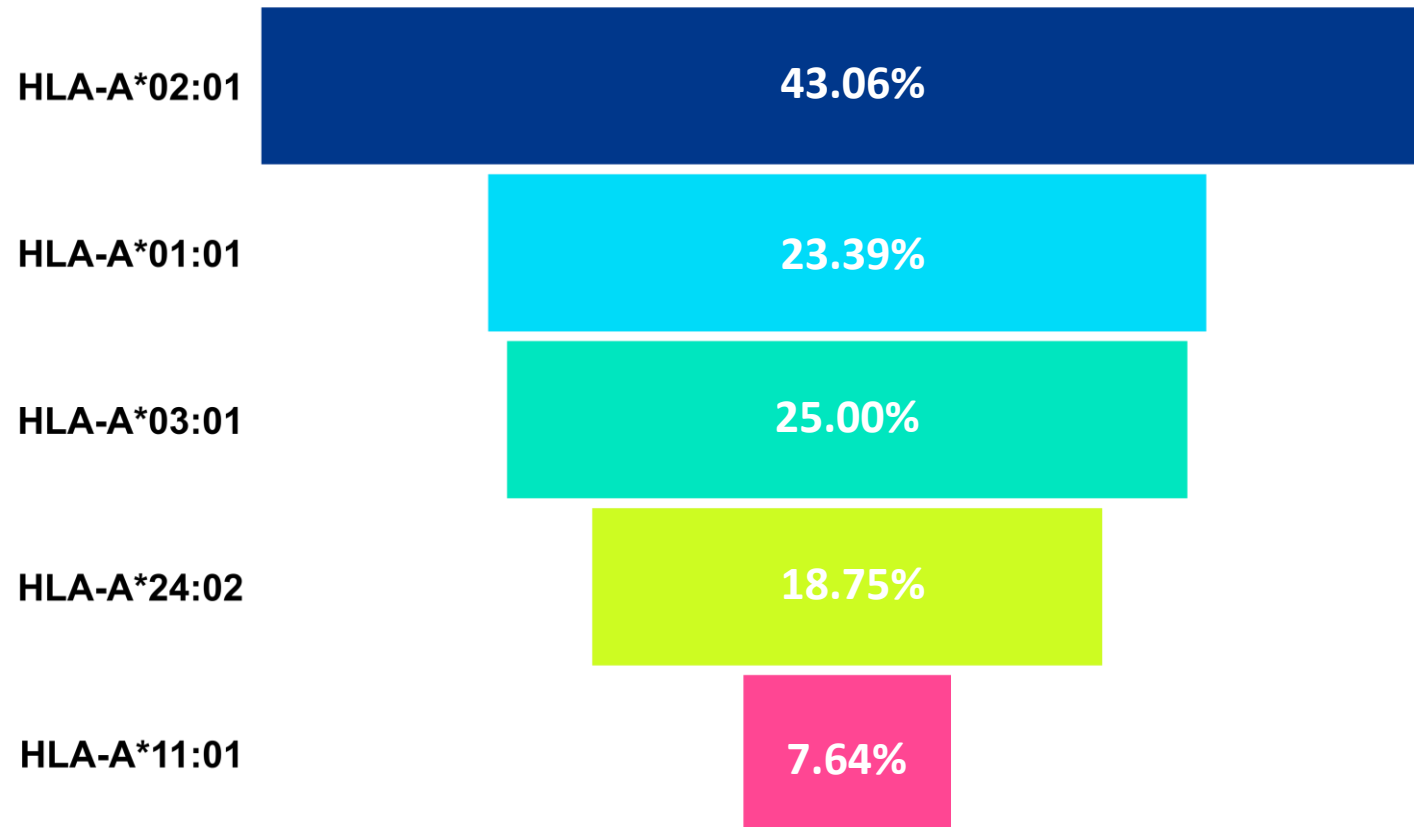
# PRAME expression can be detected more often in bone marrow compared to peripheral blood

- In alignment with disease origin and place of activity, bone marrow is positive more often than peripheral blood

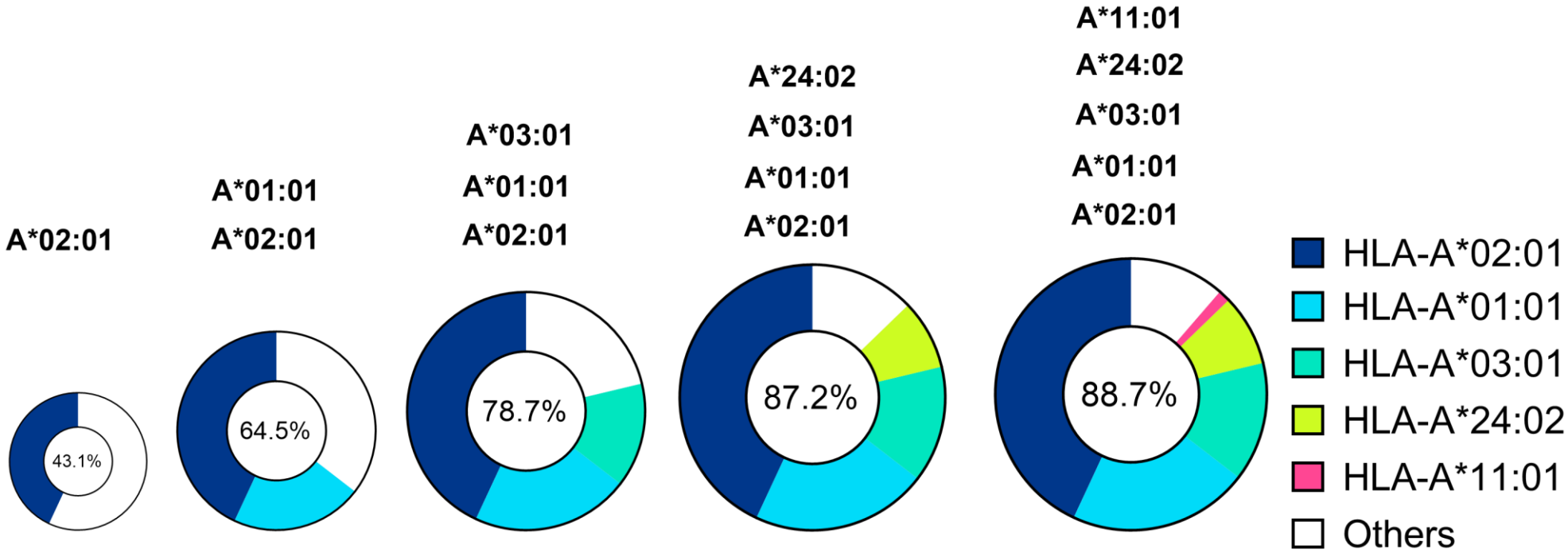


# Distribution of five most common HLA-A genotypes in the general population (Germany)

■ Analysis of 141 healthy blood donors



# TCR products addressing the five most common HLA-A allotypes can lead to coverage of approx. 88% of the population



# Co-authors

## Medigene Immunotherapies GmbH, Germany

Kathrin Davari, PhD

Silke Raffegerst, PhD

Kai Pinkernell, MD

Dolores Schendel, PhD

## Universitätsklinikums Regensburg, Germany

Simone Thomas, MD

**Thank you**

---