Serological Interference In Patients Receiving SRF231 Anti-CD47 Immunotherapy

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INTRODUCTION

- CD47 is highly expressed on RBCs as a member of the Rh-complex in the membrane.
- When CD47 binds to SIRPs on phagocytic cells it delivers a "don’t eat me" signal.
- Some cancer cells express higher levels of CD47 as a mechanism to evade immune surveillance.
- Blocking CD47 on tumor cells is thought to enhance phagocytosis and promote anti-tumor responses.

SRF231 (Surface Oncology, Cambridge MA) is a fully human anti-CD47 isotype IgG4 and has been shown to bind CD47 with high affinity.

SRF231 is in clinical trials as a single agent or with combinational therapies to treat patients with advanced solid malignancies or lymphoma.

Expression level of CD47 on RBCs varies with Rh phenotype. 1
- RhD− (rr) > RhD+ (R1R1, R2R2) > RhD+ (R2R2)
- Weakest expression on Rhnull

Anti-CD47 can bind to RBCs in-vivo and cause anemia and can interfere with serologic testing in-vitro. 3

Although SRF231 did not induce direct hemagglutination of RBCs in vitro (Peluso et al. P272 SITC 2019), interference in pre-transfusion testing is reported here.

MATERIALS AND METHODS

- CLINICAL
  - Two patients who were receiving SRF231 monotherapy.
- SEROLOGY
  - Testing was performed by tube methods with and without enhancement media or by column agglutination technology (CAT, Ortho).
  - Patient plasma samples were tested at room temperature (RT) and by indirect antiglobulin test (IAT) against cord cells, R1R1, R2R2, rr, and with -D- and Rhnull RBCs.
  - Immucor Gamma-clone anti-IgG (does not detect IgG4) and Ortho BioClone anti-IgG (total IgG) were used in IAT.
  - For adsorptions, RBCs were treated with papain.
  - Patient RBCs were treated with EDTA-Glycine Acid (EGA)
  - For titration studies, the plasma and eluate of patient 1 were diluted in PBS.
  - Adsorption studies used papain treated rr RBCs.
  - Eluates were made using Gamma ELU-KIT II (Immucor).

RESULTS

- Plasma Testing
  - In tube testing against RBCs with common Rh types plasma was:
    - Non-reactive at RT.
  - Variable reactivity in the IAT using Immucor anti-IgG:
    - Neg by LISS.
    - Neg or micro+ by PEG.
    - Micro+ to 1+ by papain.
    - Neg auto controls.
  - Strong 3+ to 4+ by all methods using Ortho anti-IgG:
    - -D- or Rhnull reacted weaker.
    - -D- 2+
    - Rhnull 1+
    - Moderately reactive with autologous controls.
  - The titer of patient 1’s sample was 16 in SAL IAT against RhD+ (R2R2) RBCs.
- Adsorption Studies
  - 3X papain-treated RhD− (rr) allo-adsorptions removed the plasma SRF231 reactivity.

REFERENCES