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Protection Against Palivizumab (Pmab) Resistant RSV with IVIG Containing High Titer Anti RSV Neutralizing Antibodies (RI-002)

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Objective: To compare the effectiveness of RI-002 and Palivizumab when administered prophylactically to cotton rats (CR) infected with Pmab resistant RSV/A/Tracy.

Methods: A Pmab resistant mutant of RSV/A/Tracy was generated by serial passage of the virus in increasing concentrations of Pmab. The Pmab-resistant mutant virus had a single amino acid mutation at position 262. This Pmab resistant mutant, infected cotton rats equally well compared to the parent virus, however, the mutant virus was resistant to the effects of Pmab immunoprophylaxis.CR were injected intraperitoneally with 1,500 mg/kg RI-002 or Pmab at 15 mg/kg activity followed by intranasal infection with the wild type or the mutant virus and viral titers were measured in lung lavage of the infected cotton rats. Virus quantification was done by semi quantitative plaque assay. RI-002 RSV- specific neutralizing antibody levels in lung lavage fluids and sera were determined by a microneutralization assay on days 0 and +4 using the wt-RSV/A/Tracy.

Results and Conclusion: RI-002 injection 24 h before RSV challenge reduced the viral counts to the wt- and PR equivalently by 2.82 and 2.45 log10 PFU/g of lung tissue, respectively while Pmab effected a reduction in the RSV titer in wt infected CR but had no effect in the CR infected with the Palivizumab resistant strain of RSV. The titers of neutralizing antibody in the sera was greater for RI-002 administered at 1,500 mg protein/kg compared to palivizumab administered at 15 mg protein/kg ($P < 0.0039$; Student t test, 2-tailed). These results suggest that RI-002 contains anti-RSV antibodies of multiple specificities which can interact even with Pmab induced escape mutants and has a neutralizing activity greater than that of Palivizumab.