The Case for Tocilizumab

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Sir,

I am delighted at the authors’ interest in my Editorial, ‘Tocilizumab or no Tocilizumab: To be or not to be. In the editorial, I have outlined the shortcomings in 5 published RCTs such as inclusion of mild COVID ARDS, insufficient sample size, mortality significantly lower than hospitalized patients’ mortality in respective countries. This implies inclusion of mild ARDS cases in these trials. There have been numerous observational studies, which have included moderately severe cases and these have reported Tocilizumab to be beneficial. I have concluded in my editorial the need to wait for results of REMAP-CAP and RECOVERY trials, which have included large number of (4871) moderately severe patients.

As of April, results of these two large, independent, multi-center RCTs on Tocilizumab are available and have shown favourable outcomes with use of Tocilizumab, (RR 0.71, 95% CI 0.52-0.96) in REMAP-CAP and (RR 0.86, 95% CI 0.77 – 0.96) in RECOVERY trial. Quoting the RECOVERY Trial, “In patients hospitalized with severe COVID, treatment with tocilizumab reduces mortality, increases the chances of successful hospital discharge, and reduces the chances of requiring invasive mechanical ventilation. These benefits are additional to those previously reported for dexamethasone. These findings require an update to clinical guidelines”. Tocilizumab is included in NICE guidelines for treatment of hospitalized severe COVID patients.

TOCIBRAS (like COVACTA, another negative RCT) has included a wide range of patients (without stratification) ranging from those with saturation <93% on ambient air (implying mild cases) to those on mechanical ventilator (severe cases comprising 16.5% patients). Also total number of patients in TOCIBRAS is only 129. A meta-analysis of 8 RCTs with 810/3268 (24.8% mortality) in Tocilizumab group against 935/ 3401 (27.5% mortality) in Standard of care (SOC), reported ratio of death rates, RR 0.87 (95% CI, 0.79 – 0.96, P=0.005).

COVINTOC another negative RCT on Tocilizumab in moderately severe COVID is from India. It included only 143 patients. Modest benefit with Tocilizumab, is not detected by RCTs with small sample size. Also in post-hoc analysis investigators of COVINTOC concluded that Tocilizumab might still be effective in severe COVID and so further studies are needed.

None of the RCTs reported higher incidence of severe infections with Tocilizumab compared to standard of care group.

The purpose of my editorial was to highlight a select group of COVID patients (moderately severe), that is likely to benefit from timely use of Tocilizumab, appropriately included in REMAP-CAP and RECOVERY trials. Both these trials have studied large number of patients and have used steroids in both groups (Tocilizumab...
and SOC group). Hence the benefit in mortality seen in both these trials can be justifiably attributed to Tocilizumab.

By avoiding use of Tocilizumab as a blanket policy, this group of moderately severe COVID patients will be denied of the modest benefit in mortality that Tocilizumab has to offer.

References