## Multiple drugs

S

### Lack of efficacy and off-label use: 2 case reports

In a report, two patients were described: a 67-year-old man exhibited lack of efficacy following off-label treatment with tocilizumab, hydroxychloroquine, azithromycin, cobicistat/darunavir and ceftazidime for SARS-CoV-2 infection. A 73-year-old man exhibited lack of efficacy following off-label treatment with tocilizumab, hydroxychloroquine, azithromycin and ceftriaxone for SARS-CoV-2 infection [*dosages not stated; not all routes stated*].

This report describes the 67-year-old man (Case 1 from the article): The man was admitted to a hospital in Italy in March 2020 with fever and respiratory failure. His medical history was significant for well controlled asthma and hypertension. Real time polymerase chain reaction assay on nasopharyngeal and throat specimens confirmed SARS-CoV-2 infection. Oxygen supply was started. He started receiving off-label treatment with hydroxychloroquine, azithromycin, cobicistat/darunavir [darunavir-cobicistat] and ceftazidime for SARS-CoV-2 infection. However, his respiratory failure rapidly worsened. He was transferred to another hospital where continuous positive airway pressure through a helmet was started. He also received off-label treatment with tocilizumab infusion for SARS-CoV-2 infection. However, further deterioration was noted, indicating lack of efficacy to tocilizumab, hydroxychloroquine, azithromycin, cobicistat/darunavir and ceftazidime. He underwent endotracheal intubation and was then transferred to the ICU where invasive mechanical ventilation was initiated. Eight days later, he was successfully extubated. He developed *Klebsiella pneumoniae* bacteraemia and septic shock of presumable pulmonary origin. He again underwent endotracheal intubation. After 5 days, he developed right tension hydro-pneumothorax requiring decompression and insertion of chest drainage. *Klebsiella pneumoniae* and *Enterococcus faecalis* were isolated from bronchoalveolar lavage. He was treated with meropenem and ampicillin. After 8 days, he was successfully weaned from mechanical ventilation. He developed persistent air leak secondary to alveolar-pleural fistula. Flexible bronchoscopy was performed. Two valves were successfully inserted into the segmentary bronchi of the middle lobe, leading to reduction in air leak. No residual air leak was detected in the following week. Once cleansing of pleural fluid was observed, drainage tube was removed successfully. In June 2020, he was transferred to the previous hospital and was then discharged a month later.

This report describes the 73-year-old man (Case 2 from the article): The man was admitted to a hospital in Italy in March 2020 with persistent fever and severe acute hypoxic respiratory failure. A nasopharyngeal swab tested positive for SARS-CoV-2. Oxygen supply was started. He started receiving off-label treatment with hydroxychloroquine, azithromycin and ceftriaxone for SARS-CoV-2 infection. On the following day, he exhibited significant worsening of gas exchange. Therefore, continuous positive airway pressure through a helmet was started. He also started receiving off-label treatment with tocilizumab infusion for SARS-CoV-2 infection. However, further worsening of his condition was noted, indicating lack of efficacy to tocilizumab, hydroxychloroquine, azithromycin and ceftriaxone. He was admitted to the ICU and invasive volume-preset mechanical ventilation was initiated. A tracheostomy was also performed. On day 15, he developed right hydro-pneumothorax, which required immediate insertion of a chest drainage tube. *Klebsiella pneumoniae* and *Enterococcus faecalis* were isolated from pleural fluid which were successfully treated with meropenem and ampicillin. After 1 month, his clinical condition improved markedly and he was weaned from mechanical ventilation. He developed persistent air leak secondary to alveolar-pleural fistula. He was transferred to the ICU where flexible bronchoscopy was performed. Three valves were inserted into the segmental bronchi of the right lower lobe. A gradual reduction of air leak was observed followed by resolution. Thereafter, the drainage tube was removed and he was discharged on July 2020.

Donatelli P, et al. Endobronchial valve positioning for alveolar-pleural fistula following ICU management complicating COVID-19 pneumonia. BMC Pulmonary Medicine 21: No. 1, 2021. Available from: URL: http://doi.org/10.1186/s12890-021-01653-w

803660916