

HTA - - Health Technology Assessment Report

# Riociguat for the treatment of Phe508del homozygous adults with cystic fibrosis.

Code: PM34419414

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## Study design (if review, criteria of inclusion for studies)

1) TIGER-1; NCT00357279; 08-108; denufosal vs placebo; phase III. Completed and published in abstract; 2) NCT00056147; 08-103; denufosal vs placebo; phase II. Complete and published; 3) TIGER-2; NCT00625612; 08-110; CF; denufosal vs placebo; phase III. Trials registry; 4) Extension of TIGER-2; NCT00846781; 08-114; denufosal; phase III. Trials registry.

## List of included studies (4)

1) TIGER-1; NCT00357279; 2) NCT00056147; 3) TIGER-2; NCT00625612; 4) Extension of TIGER-2; NCT00846781

## Participants

1) n=352;  $\geq 5$  years old; CF; FEV1  $\geq 75\%$  predicted; stable with no acute pulmonary exacerbations for at least 4 weeks. 2) n=89; 8-50 years old; CF; FEV1  $\geq 75\%$  predicted; oxyhaemoglobin saturation  $\geq 90\%$ ; clinically stable. 3) n=450;  $\geq 5$  years old; CF; FEV1  $\geq 75\%$   $\geq 110\%$  predicted; reproducible spirometry; stable with no acute pulmonary exacerbations for at least 4 weeks. 4) n=380; completed TIGER-2 study.

## Interventions

1) Randomised to nebulised denufosal 60mg or placebo three times daily for 24 weeks. All enter 24 week open-label denufosal extension. 2) Randomised to nebulised denufosal 20, 40 or 60mg or placebo three times daily for 28 days. 3) Randomised to nebulised denufosal 60mg or placebo three times daily for 12 months. 4) All participants given nebulised denufosal 60mg three times daily for other 12 months.

## Outcome measures

1) primary outcome: Lung function; secondary outcomes: Pulmonary exacerbation requirement for concomitant CF medications, quality of life (QoL). 2) primary outcome: Lung function (FEV1, FVCb, FEV1/FVC and FEF25%-75%); secondary outcomes: Respiratory symptoms, sputum weight, pulmonary exacerbations, high-resolution computed tomography (hyperinflation, mucus plugging, peribronchial thickening, bronchiectasis, ground glass, opacity and cysts/bullae). 3) primary outcome: Lung function; secondary outcomes: Pulmonary exacerbation, antibiotic use, incidence of hospitalisation or emergency room visits, health resource utilisation, QoL. 4) primary outcome: Lung function; secondary outcomes: Pulmonary exacerbation, antibiotic use, incidence of hospitalisation or emergency room visits.

## Main results

1) At week 24: adjusted mean change in FEV1 of 48ml vs 3ml ( $p=0.047$ ) for denufosal and placebo respectively. Difference compared to placebo in mean change in FEV1 of 41ml ( $p=0.101$ ) in patients with no exacerbation vs 101 ml with exacerbation ( $p=0.062$ ). Most common AEs for denufosal and placebo respectively: Cough: 55% vs 59%, nasal congestion 15% vs 19%, pharyngolaryngeal pain 19% vs 18%, rhinorrhea 10% ( $p$

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## See also

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## Keywords

Other drugs; denufosal; Inhalation OR nebulised; pharmacological\_intervention;