05.01 - Airway pharmacology and treatment

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Masitinib in severe asthma: Results from a randomized, phase 3 trial

Severe asthma, Asthma - management, RCT (Randomized Controlled Trial)

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BACKGROUND:

Study AB07015 evaluated oral masitinib (6 mg/kg/d) in severe persistent asthma, uncontrolled by high-dose ICS/LABA and oral corticosteroids (OCS) (≥7.5 mg/d), irrespective of baseline eosinophil levels.

METHOD:

Eligible adult patients (pts) were treated for 36 weeks (with possible blinded extension until at least week-96). Primary endpoint was reduction of annualized severe asthma exacerbation rate (SAER) for overall exposure (W0–W96). A key subgroup was defined as pts with initial eosinophil count of ≥150 cells/µL (EOS). Subgroup analysis according to cumulative OCS intake was also performed, a higher dose indicating more severe asthma that is harder to control.

RESULTS:

MAS (n=240) showed a significant 35% reduction in SAER relative to placebo (PBO, n=115) with a rate ratio (RR) of 0.64 ([95%CI[0.47–0.90];p=0·0103]). For the EOS subgroup, MAS (n=181) showed a significant 38% reduction in SAER (n=87); RR=0.62 ([95%CI[0.42–0.91];p=0·0156). Benefit of MAS increased in pts who had a higher cumulated use of OCS (**see Table**). In pts receiving an annualized cumulative OCS intake of >1000 mg, SAER was significantly reduced by 51% in the primary analysis population (p=0·0060), and by 71% in the EOS subgroup (p=0·0003). Safety was consistent with the known MAS profile and no new safety signals were observed. Incidence of ≥1 adverse event was 83.4% for MAS vs 82.0% for PBO.

CONCLUSION:

Masitinib demonstrated a positive benefit/risk ratio in uncontrolled severe asthma, regardless of baseline eosinophil level. Benefits were greatest in pts with the highest OCS dose dependency.

Table: Analysis of severe asthma exacerbation rates (SAER) according to prior cumulative OCS intake

Treatment group (n)	Exposure, mo	RR [95% CI]	Reduction	P-value
Primary analysis population				
Cumulative OCS >500 mg				
Masitinib (161)	13.8	0.59 [0.39, 0.88]	41%	0.0092
Placebo (82)	14.4			
Cumulative OCS >1000 mg				
Masitinib (120)	13.9	0.49 [0.29, 0.82]	51%	0.0060
Placebo (66)	15.2			
Cumulative OCS >1500 mg				
Masitinib (89)	14.5	0.43 [0.21, 0.88]	57%	0.0203
Placebo (52)	15.2			
EOS subgroup				
Cumulative OCS >500 mg				
Masitinib (127)	13.4	0.51 [0.39, 0.88]	49%	0.0049
Placebo (60)	13.9			
Cumulative OCS >1000 mg				
Masitinib (92)	13.3	0.29 [0.29, 0.82]	71%	0.0003
Placebo (46)	15.2			
Cumulative OCS >1500 mg				
Masitinib (69)	13.9	0.28 [0.21, 0.88]	72%	0.0032
Placebo (38)	15.5			

EOS subgroup: pts with a baseline eosinophil count of ≥150 cells/µL. OCS: oral corticosteroid (cumulative intake in the 12 months prior to screening); SAER: annualized severe asthma exacerbation rate. Severe exacerbation event defined as worsening asthma leading to an increase from stable maintenance dose of corticosteroids for ≥3 days or hospitalization.