Introduction
Major depressive disorder (MDD) is often associated with various psychiatric comorbidities as for example anxiety symptoms. Adequate antidepressant (AD) treatment in this comorbid population is important due to higher severity of the disease and a worse prognosis for the therapeutic outcome (1-3). Aim of the presented subgroup-analysis of two non-interventional-studies was to evaluate effectiveness and tolerability of agomelatine in patients with MDD and comorbid anxiety symptoms. The post-hoc defined subgroup had been selected due to representative patient numbers of daily practice and clinical relevance

Methods
Patients: The presented pooled data (n=4394) are based on two German non-interventional studies over 12 weeks (W12). VIVALDI (n=3324) and VIVALDI-Praxis (n=1070). Outpatients >18 yrs with first or recurrent depressive episode were analysed in the total population and the subgroup of patients who reported comorbid anxiety symptoms or panic disorder at baseline (n=956). Patients were treated with agomelatine 25 mg/once daily at bedtime with dose increase, if necessary.

Methods: Antidepressant effects were documented by short-version Montgomery-Asberg Depression-Rating-Scale (svMADRS) and Clinical-Global-Impression Scale; AD at baseline and response to agomelatine (CGI-I≤2) or remission (CGI-S=1 or 2) after 12 weeks (final visit). According to CGI, 77.4% /70.7% (TP/ANX) responded to agomelatine-treatment (CGI-I≤2) and 32.0% /22.7% were classified as remitters (CGI-S=1 or 2) after 12 weeks. According to CGI, 77.4% /70.7% (TP/ANX) responded to agomelatine-treatment (CGI-I≤2) and 32.0% /22.7% were classified as remitters (CGI-S=1 or 2) after 12 weeks. The incidence of ADR reveals slight differences in respect to psychotropic/somatic co-medication with higher incidence in co-medicated patients in ANX. ADR were documented for patients with (8.8% / 11.8%) or without (8.0% / 8.6%) psychotropic drugs and with (8.2% / 12.5%) or without (8.3% / 8.2%) somatic co-medication for TP / ANX respectively. Overall, clinically relevant transaminase elevations were comparable (0.4% / 0.7%).

Results
a) Baseline Data
21.8% of the total population (TP) with MDD reported comorbid anxiety or panic disorder (ANX). Patients characteristics were comparable between both groups TP / ANX with a majority of females (64.9% / 66.1%) and mean age (50.7 / 49.7). More frequently recurrent depressive episodes (62.6% / 73.1%), AD-pretreatment (64.1% / 80.9%), co-medication with AD (21.7% / 32.7%) or co-medication with other psychotropic drugs (30.0% / 38.1%) were apparent in ANX, reflecting the higher severity of disease. No major imbalance was apparent in somatic comorbidities (59.2% / 58.6%) and somatic co-medication (43.0% / 38.6%).

b) Antidepressant effect
At study-start patients of both groups showed moderate depression (svMADRS total-score 31.4 / 31.8), with a small difference of improvement over 12 weeks (14.3 / 12.2 points on svMADRS-score). 69.3% / 63.2% of TP / ANX were classified as responders (≥50% reduction of svMADRS) and 57.2% / 46.9% showed remission (svMADRS≤12) after 12 weeks (final visit). Overall, AD treated responders to agomelatine-treatment (CGI-I≤2) and 32.0% / 22.7% were classified as remitters (CGI-S=1 or 2) after 12 weeks.

c) Tolerability
Overall, ADR were reported in 8.2% / 9.8% of TP / ANX, mainly headache, nausea, dizziness and diarrhoea, and sADR in 0.23% / 0.31% (headache, diarrhoea, psychiatric disorder). The incidence of ADR reveals slight differences in respect to psychotropic / somatic co-medication with higher incidence in co-medicated patients in ANX. ADR were documented for patients with (8.8% / 11.8%) or without (8.0% / 8.6%) psychotropic drugs and with (8.2% / 12.5%) or without (8.3% / 8.2%) somatic co-medication for TP / ANX respectively. Overall, clinically relevant transaminase elevations were comparable (0.4% / 0.7%). Mean weight and BMI remained unchanged in both groups.

Conclusion
In the cohort of depressed patients with comorbid anxiety or panic symptoms, agomelatine was associated with comparable improvement of depressive symptoms (svMADRS, CGI). Agomelatine showed good tolerability with / without psychotropic and /or somatic co-medication in routine practice over 12 weeks.