While the study design and differences in sample sizes does not allow formal comparisons between the double- and single blinded groups, the exploratory comparator, Voltaren QID, did not reach statistically significant differences to placebo or AMZ001 in any of the endpoints, in neither the ITT nor the subgroup analyses. The safety and tolerability of AMZ001 was favorable, as the frequency of AEs leading to discontinuation of treatment was similarly low (ranging between 2.8 % to 6.6 %) between AMZ001 once or twice daily and placebo or Voltaren Gel 1%. The most common treatment-emergent AEs were application site dryness, and application site erythema. No serious adverse events were reported during the trial.

Conclusion: AMZ001, a novel topical diclofenac formulation, either once or twice daily was efficacious in the treatment of knee OA pain with a good tolerability and safety profile, suggesting AMZ001 may be a promising alternative to existing pain-relieving treatments in knee OA.

References: NA

Disclosure of Interests: Asger Bihlet Shareholder of: Nordic Bioscience, Consultant of: Amzell BV, Medivir AB, Xintela AB, Merck KGaA, Employee of: Nordic Bioscience, Inger Byrjalsen Employee of: Nordic Bioscience, Henning Bay Nielsen: None declared, Jeppe Andersen Shareholder of: Minor shareholder of Nordic Bioscience, Consultant of: Medivir AB, Xintela AB, Employee of: Nordic Bioscience, Laetitia Delpy Employee of: Amzell BV, Caroline Derne Employee of: Amzell BV, Dario Carrara Employee of: Amzell BV

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AB0857 A NEW BIOPSYCHOSOCIAL QUESTIONNAIRE FOR PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: OA is a problem that cartilage damage occurs, which leads to stiffness in the joint, pain and functional limitations (1). This problem can also cause psychosocial impact like other chronic diseases (2). As with other rheumatic diseases, this complex picture of inflammation required biopsychosocial approaches and measurement methods for knee OA.

Objectives: This study was planned to investigate the validity and reliability of a new biopsychosocial questionnaire which is named Cognitive Exercise Therapy Approach Biopsychosocial Questionnaire (BETY-BQ) in individuals with knee osteoarthritis (OA).

Methods: The study included 150 individuals who diagnosed knee osteoarthritis at stage 1 or 2 according to the Kellgren-Lawrence scale. For determining daily living activities; Health Assessment Questionnaire (HAQ), for quality of life Short Form-36 (SF-36) Quality of Life Scale, for anxiety and depression levels; Hospital Anxiety and Depression Scale (HADS), for severity of disease Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and for biopsychosocial evaluation BETY-BQ were used.

Results: The correlation between BETY-BQ and other scales was examined by Spearman correlation analysis ($r=-0.252, 0.633, p<0.05$). Cronbach's alpha coefficient and item-total correlation were used as reliability methods. Cronbach's alpha coefficient was examined for the internal consistency of the scale and was found to be 0.887 for the first evaluation, 0.917 for measurements after 1 week and 0.843 for measurements after 3 months. Item total correlation, which was another indicator of reliability, ranged from 0.632 to 0.854 ($p<0.05$).

Table 1. Correlation coefficients between all questionnaires and Cognitive Exercise Therapy Approach Biopsychosocial Questionnaire (BETY-BQ).

Spearman Correlation Analysis	Cognitive Exercise Therapy Approach Biopsychosocial Questionnaire (BETY-BQ)	
	r	p
WOMAC-Pain	0,473	<0,001
WOMAC-Stiffness	0,458	<0,001
WOMAC-Physical Function	0,514	<0,001
WOMAC-Total Score	0,553	<0,001
hospital anxiety and depression scale- anxiety	0,615	<0,001
hospital anxiety and depression scale-depression	0,252	0,002*
Health Assessment Questionnaire	0,633	<0,001
Short Form-36 Role limitations due to physical health	-0,440	<0,001
Short Form-36 Role limitations due to emotional problems	-0,357	<0,001
Short Form-36 Physical functioning	-0,469	<0,001
Short Form-36 Social functioning	-0,355	<0,001
Short Form-36 Pain	-0,487	<0,001
Short Form-36 General Health	-0,513	<0,001
Short Form-36 Emotional well-being	-0,508	<0,001
Short Form-36 Energy/fatigue	-0,453	<0,001

Conclusion: As a result of our study, it was concluded that BETY-BQ is a valid and reliable biopsychosocial questionnaire in individuals with knee OA diagnosis. This result showed that BETY-BQ can be used in clinics to evaluate biopsychosocial involvement in patients with knee OA.

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AB0858 TREATMENT ALGORITHM FOR ANKLE OSTEOCHONDRAL LESIONS AND DEFECTS

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Background: traumatic ankle joint osteochondral lesions and defects (OHL) is frequent cause of OA, chronic pain and loss of joint function; results of traditional treatment strategy are often unsatisfying

Objectives: to develop treatment algorithm for OHL based on evaluation of previously determined main prognostic factors.

Methods: the analysis of long-term (36 ± 4.5 months) treatment results of 239 patients after traumatic ankle joint OHL revealed the following factors with the greatest predictive value (defined by PC – prognostic coefficient) for good result of treatment (defined as AOFAS function score 75-100 points): age < 40 years ($PC = 8.5$); size of OHL $\leq 1.0\text{cm}^2$; volume $\leq 1.5\text{cm}^3$ ($PC = 8.0$); osteoarthritis stage $\leq II$ ($PC = 7.2$). Based on these factors, a step-by-step, discrete and alternative algorithm for the choice of treatment tactics was created. The algorithm includes use of arthroscopic or open debridement, abrasive chondroplasty, bone marrow regeneration stimulation (microfracturing or tunneling), mosaic osteochondroplasty, arthroplasty or arthrodesis, the use of cellular regenerative technologies (bone marrow cells, platelet riched plasma), and others. Patients of older age with advanced OA need complex, step up approach, surgical treatment combined with regenerative cell technologies. The effectiveness of the differentiated approach to treatment was studied in 72 patients with OHL (main group) in comparing to 72 patients in whom traditional treatment approaches were used, based on the stage of injury according to the Berndt & Hardy classification (comparison group).

Results: compared to the traditional approach, the developed algorithm and treatment system allowed to half terms of hospitalization, to reduce the intensity of pain syndrome (by NRS) and increase the functional activity (by AOFAS) by 25%. In 3 years after trauma good/excellent results of treatment demonstrated 86% patients of main group and 32,2% of patients from comparing group ($p<0.05$).

Conclusion: implementation of the developed treatment algorithm increases the number of good and excellent long-term results by 2.6 times and reduces the number of complications and unsatisfactory results by 4.9 times.

Disclosure of Interests: None declared

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AB0859 IMPROVEMENTS IN PHYSICAL FUNCTION IN PATIENTS WITH OSTEOARTHRITIS RECEIVING SUBCUTANEOUS TANEZUMAB IN 3 RANDOMIZED CONTROLLED TRIALS

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Background: Tanezumab, a monoclonal antibody against nerve growth factor, is in development for the treatment of the signs and symptoms of osteoarthritis (OA).

Objectives: To assess the improvement in physical function following treatment with subcutaneous (SC) tanezumab in three Phase 3 OA studies.

Methods: All three randomized, double-blind, controlled studies enrolled patients (pts) with radiographically-confirmed OA of the hip or knee, who had inadequate response or could not tolerate standard of care analgesics. Study 1 was a dose-titration study (NCT02697773), where pts received two SC doses of: placebo at baseline/week (wk) 8; tanezumab 2.5mg at baseline/wk 8; or

tanezumab 2.5 mg at baseline/5 mg at wk 8¹. In Study 2 (NCT02709486), pts received three SC doses of placebo, tanezumab 2.5 mg, or 5 mg (at baseline/wk 8/wk 16). In Study 3 (NCT02528188), pts received a stable dose of nonsteroidal anti-inflammatory drugs (NSAIDs) before randomization to double-dummy tanezumab 2.5 mg or 5 mg (at baseline and every 8 wks during a 56 wk treatment period) or twice daily oral NSAIDs. Pts completed Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Physical Function subscale questionnaires in clinic. The least squares (LS) mean (standard error (SE)) change from baseline was calculated for each timepoint up to wk 16 and significance was calculated versus placebo (Studies 1 and 2) or NSAID (Study 3).

Results: A total of 4541 pts were evaluated (n=696 in Study 1, n=849 in Study 2 and n=2996 in Study 3). In Studies 1 and 2, there were statistically significant improvements from baseline for all tanezumab treated groups versus placebo at wks 2, 4, 8, 12 and 16 (**Table 1**). In Study 3, the tanezumab 2.5 mg group showed a significant improvement from baseline at wk 2, compared with the NSAID group (**Table 2**). At wk 4, both tanezumab treatment groups showed a significant improvement from baseline compared with the NSAID group (**Table 2**). The tanezumab 5 mg group showed a significant improvement from baseline compared with the NSAID group at wks 8 and 16 (**Table 2**).

Table 1. Change from baseline in WOMAC Physical Function: Study 1 and 2

		Study 1			Study 2		
		Tanezumab 2.5 mg n=231	Tanezumab 2.5/5 mg n=233	Placebo n=232	Tanezumab 2.5 mg n=283	Tanezumab 5 mg n=282	Placebo n=282
Wk 2	LS mean (SE)	-2.89 (0.21)	-3.05 (0.21)	-2.14 (0.21)	-1.95 (0.14)	-1.69 (0.14)	-1.26 (0.14)
	p vs placebo	0.0004	<0.001		<.0001	0.0014	
Wk 4	LS mean (SE)	-3.30 (0.21)	-3.38 (0.21)	-2.28 (0.21)	-2.52 (0.15)	-2.50 (0.15)	-1.71 (0.15)
	p vs placebo	<.0001	<.0001		<.0001	<.0001	
Wk 8	LS mean (SE)	-3.17 (0.21)	-3.12 (0.21)	-2.55 (0.21)	-2.38 (0.15)	-2.52 (0.15)	-1.76 (0.15)
	p vs placebo	0.0057	0.0114		<.0001	<.0001	
Wk 12	LS mean (SE)	-3.61 (0.22)	-3.80 (0.22)	-2.75 (0.22)	-2.83 (0.16)	-2.87 (0.16)	-2.04 (0.16)
	p vs placebo	0.0004	<.0001		<.0001	<.0001	
Wk 16	LS mean (SE)	-3.22 (0.22)	-3.45 (0.22)	-2.56 (0.22)	-2.68 (0.16)	-2.69 (0.16)	-2.02 (0.17)
	p vs placebo	0.0065	0.0002		<.0001	<.0001	

Table 2. Change from baseline in WOMAC Physical Function in Study 3

		Tanezumab 2.5 mg n=1002	Tanezumab 5 mg n=998	NSAID n=996
Wk 2	LS mean (SE)	-1.76 (0.08)	-1.64 (0.08)	-1.55 (0.08)
	p vs NSAID	0.0150	0.3286	
Wk 4	LS mean (SE)	-2.29 (0.09)	-2.31 (0.09)	-1.96 (0.09)
	p vs NSAID	0.0004	0.0001	
Wk 8	LS mean (SE)	-2.46 (0.10)	-2.69 (0.10)	-2.27 (0.10)
	p vs NSAID	0.0517	<.0001	
Wk 16	LS mean (SE)	-3.27 (0.11)	-3.39 (0.11)	-3.08 (0.11)
	p vs NSAID	0.0691	0.0030	

Conclusion: Consistent improvements in WOMAC Physical Function were seen across the first 16 wks for all dose groups of tanezumab-treated pts versus placebo in Study 1 and 2. The tanezumab 5 mg group in Study 3 showed a significant improvement at wks 4, 8 and 16 compared with the NSAID group. Improving physical function could help OA pts attain treatment goals beyond pain relief, improving their ability to perform important daily activities.

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AB0860

STUDY DESIGN OF ROCCELLA: A PHASE 2 CLINICAL TRIAL WITH A DISEASE-MODIFYING OSTEOARTHRITIS DRUG CANDIDATE GLPG1972/S201086

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Background: Loss of articular cartilage is one of the major signs of osteoarthritis (OA). Aggrecan, the main proteoglycan component of the extracellular matrix of articular cartilage is cleaved by ADAMTS-5 (A Disintegrin And Metalloproteinase with Thrombospondin-motif-5).¹ GLPG1972/S201086, a potent and highly selective inhibitor of ADAMTS-5, is an oral Disease-Modifying Osteoarthritis Drug (DMOAD) candidate. In a pooled Phase 1 safety analysis involving 171 participants GLPG1972/S201086 was shown to be well tolerated.

Objectives: To present the study design of ROCCELLA, a large Phase 2 clinical trial in knee OA (KOA) patients, evaluating the efficacy and safety of GLPG1972/S201086 in reducing cartilage loss in OA.

Methods: ROCCELLA is a multinational 52-week, multicentre randomized double-blind placebo-controlled dose-ranging phase 2 trial for the treatment of OA (NCT03595618). Eligible patients were aged 40–75 years with a diagnosis of primary femorotibial KOA, a pain score of 40–90 mm on a 100 mm Visual Analogue Scale (VAS), predominant medial disease and a combined Kellgren/Lawrence (KL) 2 or 3 and Osteoarthritis Research Society International (OARSI) medial joint space narrowing (JSN) 1 or 2 severity grading range upon central reading of the X-ray. If both knees were eligible, the target knee was selected based first on the highest KL grade, then on the highest JSN grade and finally on the highest pain VAS score at baseline. Patients were randomized 1:1:1:1 to take placebo or three dose levels of GLPG1972/S201086 orally once daily for 52 weeks. The target knee was evaluated by quantitative Magnetic Resonance Imaging (qMRI) at baseline visit, week 28 and week 52, or at early withdrawal.

The primary endpoint of the study is change from baseline to week 52 in cartilage thickness of the central medial tibio-femoral compartment (cMTFC) of the target knee. Secondary objectives are safety and tolerability including treatment emergent serious adverse events. Additional secondary structural and clinical efficacy objectives are based on changes from baseline in the target knee: cartilage thickness and bone area on qMRI, KOA "progressor" rates, Joint Space Width on X-ray, pain VAS, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total and sub scores, Patient Global Assessment VAS and the proportion of Outcome Measures in Rheumatology (OMERACT)-OARSI responders. Blood will be collected to assess the pharmacokinetics of GLPG1972/S201086. Planned, exploratory analyses include biochemical biomarkers of cartilage and bone turn-over. The study is designed to maintain the experiment wise type I error at 5%. A Mixed-effects Model for Repeated Measures will be used for the primary analysis. The randomisation was stratified by geographic region.

Results: The study started in August 2018 and was fully recruited (N=938) by June 2019. Large numbers of patients with KOA had to be screened to meet the stringent pre-specified selection criteria. The study completion is expected by end of 2020.

Conclusion: This is the first large Phase 2 study where patients with primary KOA are treated for 52 weeks with GLPG1972/S201086, an orally administered DMOAD candidate. This clinical trial was designed with a combination of two radiological selection criteria to ensure sufficient structural progression (cartilage loss) in the study population.

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