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ORAL ABSTRACTS

322.DISORDERS OF COAGULATION OR FIBRINOLYSIS: CLINICAL AND EPIDEMIOLOGICAL

Surgical Procedures and Hemostatic Outcome in Patients with Hemophilia Receiving Concizumab Prophylaxis during the Phase 3 explorer7 and explorer8 Trials

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Introduction
Concizumab is an anti-tissue factor pathway inhibitor monoclonal antibody that has been developed for once-daily subcutaneous prophylactic treatment for hemophilia of all subtypes. The phase 3 explorer7 (NCT04083781) and explorer8 trials (NCT04082429) investigated the efficacy and safety of concizumab prophylaxis in patients with hemophilia A or B with (HAwI/HBwI, explorer7) or without (HA/HB, explorer8) inhibitors.
Aim
To provide an overview of any surgical procedures at the 56-week cut-off performed on patients who received concizumab prophylaxis in the explorer7 and explorer8 trials.
Methods
Patients in both explorer7 and explorer8 trials were exposed to no prophylaxis (arm 1) or concizumab prophylaxis (arms 2-4) based on their treatment regimen before the trial. After the main part of the trial, all patients (arms 1-4) could continue in the extension part of the trial receiving concizumab for up to 136 weeks. Informed consent/ethics committee approvals were obtained as appropriate. Minor surgical procedures (defined as any invasive operative procedure where only the skin, mucous membranes or superficial connective tissue is manipulated) were permitted during the explorer7 and explorer8 trials, and management of minor surgeries was at the investigator's discretion. Planned major surgery was not permitted, and for any cases of acute major surgery, a concizumab pause was recommended. Data regarding both minor and major surgeries undertaken in patients were collected at the 56-week cut-off of the trials. Local/topical use of anti-fibrinolytics was permitted during surgical procedures in both trials (single systemic doses allowed following benefit-risk evaluation) and patients undergoing minor surgical procedures continued to receive concizumab prophylaxis during the perioperative period (with no change to the dosage they received).
Results
During both trials, a total of 278 patients received concizumab prophylaxis. Of these, 30 patients underwent a minor surgical procedure, including 6 (20.0%) adolescents (aged 12-17 years) and 24 (80.0%) adults (aged 18-64 years). Nine patients who underwent a minor procedure had HA (30.0%), 10 had HB (33.3%), 7 had HAwI (23.3%) and 4 had HBwI (13.3%). Four patients underwent both major and minor surgeries and 2 patients underwent major surgeries only. In total, 44 surgical procedures were undergone in 32 patients. The surgical procedures that were performed in patients who received concizumab included a range of minor surgeries in both trials (including tooth extractions and other dental procedures, port removal, colonoscopy, arthrodesis and urethral augmentation). Overall, 6 cases of major surgery were reported during the explorer7 and explorer8 trials (left hip arthropathy, hematoma drainage, right femoral neck fracture, total knee arthroplasty, right ankle arthropathy and diagnostic laparoscopy with removal of blood from the abdominal cavity) in 1 patient with HA, 2 patients with HB, 1 patient with HAwI and 2 patients with HBwI respectively.

Bleeding episodes related to minor and major surgical procedures (n=30) were reported in 24 patients and in 15 of these a total of 17 bleeding episodes were treated. The majority of patients (n=12) who reported a treated surgical-related bleeding episode had undergone a dental surgical procedure. Other minor surgical procedures with associated bleeding episodes included port removal, and venesection. The number and type of minor surgical procedures are further described in Table 1.

Conclusion

Minor surgical procedures were conducted in approximately 11% of patients who received treatment with concizumab during the phase 3 explorer7 and explorer8 trials. Most minor surgeries that took place were dental procedures and the majority of surgical-related bleeding episodes were mild or moderate. Overall, minor surgeries could be performed on patients with hemophilia under concizumab prophylaxis.

Disclosures Barnes: *Roche:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Novo Nordisk:* Membership on an entity's Board of Directors or advisory committees; *CSL Behring:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Speakers Bureau. **Mathias:** *Novartis:* Research Funding; *Bayer:* Honoraria; *Sobi:* Honoraria, Research Funding; *Octapharma:* Honoraria, Other: Reimbursement for attending meetings , Research Funding; *Roche:* Honoraria, Other: Reimbursement for attending meetings , Research Funding; *Novo Nordisk:* Honoraria, Research Funding; *Sanofi:* Research Funding; *Takeda:* Honoraria, Other: Reimbursement for attending meetings , Research Funding; *CSL:* Honoraria, Other: Reimbursement for attending meetings ; *Pfizer:* Research Funding. **Linari:** *CSL Behring:* Membership on an entity's Board of Directors or advisory committees; *Roche:* Membership on an entity's Board of Directors or advisory committees; *Sobi:* Speakers Bureau; *Novo Nordisk:* Membership on an entity's Board of Directors or advisory committees. **Hvitfeldt Poulsen:** *Novo Nordisk:* Honoraria; *Sobi:* Honoraria; *Roche:* Membership on an entity's Board of Directors or advisory committees. **Bovet:** *Novo Nordisk:* Current Employment. **Odgaard-Jensen:** *Novo Nordisk A/S:* Current Employment. **Matsushita:** *Takeda, Bayer, Novo Nordisk, Chugai Pharmaceutical Co., Ltd, Pfizer:* Speakers Bureau; *Takeda, Bayer, Sanofi, Chugai Pharmaceutical Co., Ltd, CSL, JB, KMB, Novo Nordisk, Fujimoto, Sysmex:* Honoraria; *Chugai Pharmaceutical Co., Ltd, Novo Nordisk:* Research Funding; *Bayer:* Consultancy.

Table 1. Types of minor surgical procedures in patients exposed to concizumab and on treatment (all treatment arms) during explorer7 and explorer8 by surgery and hemophilia type (safety analysis set at 56-week cut-off)

	Minor surgery			
	HA	HAwI	HB	HBwI
Pts who underwent surgical procedure, n	9	7	10	4
Total number of surgical procedures	13	10	11	4
Dental procedure	6	5	7	2
Arthrodesis	0	0	1	0
Colonoscopy	2	0	0	0
Other*	1	2	2	2

*Other surgeries included port removal, embolization, tongue mucus membrane injury, phimosis, venesection, pyoderma, urethral augmentation and hyaluronic acid infiltration. HA, hemophilia A without inhibitors; HAwI, hemophilia A with inhibitors; HB, hemophilia B without inhibitors; HBwI, hemophilia B with inhibitors; Pts, patients.

Figure 1

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