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Pan-European Pharmaceuticals

Feedback from FY24 doc series: Novartis' Iptacopan (C3G, IgAN). Scemblix 1L CML

Industry Overview

16 January 2024

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Feedback from, C3G, IgAN, CML pipe physician call

We provide feedback from our first FY24 pipeline physician call focussing on Novn's Iptacopan (C3G, IgAN) & Scemblix CML, part of our FY24 pipeline doc call series.

C3G high unmet need. Iptacopan could see rapid uptake

Our physician saw C3G as a large unmet need with no approved or effective therapies and 50-70% of patients progressing to ESRD. He was positive on Iptacopan, noting it acts directly through the alternate pathway that drives the disease. Sees PII c50% proteinuria reduction as highly clinically relevant a good predictor of eGFR (kidney function-secondary endpoint) benefit, and likely to satisfy regulators. Saw potential to see efficacy in eGFR secondary endpoint at primary 6-month endpoint given C3G is a faster progressing disease than IgAN. Doesn't expect different PIII outcomes(see note) across C3G sub-types C3GN and DDD) given both driven by alternate pathway. Our physician expects rapid adoption, given a population of patients with no approved therapy, and could see pool of diagnosed patients increase. Sees Apellis' Empaveli (PIII 24E) very similar from a clinical profile perspective but would prefer oral administration (Iptacopan). Also noted positive read-across to recently started Iptacopan IC-MPGN PIII (data 26E).

IgAN more crowded, but opps for Iptacopan / Atrasentan

Saw IgAN as much more crowded, though a larger population with 110k US patients, and 1M in China. Focused on: 1) Iptacopan: Saw proteinuria reduction in PII as sufficient to predict eGFR slope benefit in PIII. Although Travere's Filspari didn't meet its eGFR endpoint, despite strong proteinuria redn, noted this was due to better performance of the control arm than expected. Given expected boxed warning for need for vaccination against encapsulated bacterial infections and pricing for ultra-rare indications, expects use in very late line patients only, with mid-single digit % overall penetration (BofAe 5%). 2) Our KOL was excited about Atrasentan as an effective (55% 24-week proteinuria reduction) non-immunosuppressive option, expecting to use it in 2L, after ACE/SGLT2. Doesn't expect to see boxed warning for liver tox (Filspari has) and doesn't see oedema or heart failure risk (that was seen in DKD sonar study) given a much younger, healthier population. 3) Optimistic APRIL inhibitor given potential for disease modification.

Scemblix could see rapid adoption in 1L CML

Our physician saw Scemblix as a possible replacement for his 1L CML use of Sprycel (uses in c90% of patients) with potential use shifting to c70% Scemblix (vs 30% in our model), 20% on Sprycel and 10% on Gleevec post launch, given better efficacy and tolerability(see note). Noted 30% of Sprycel treated patients have significant AE's, although only 10% of these discontinue. Sees Scemblix as very effective based on use in the 3L and T315I settings, and milder AE profile. Thinks 25-30% better MMR relative to existing agents in detailed ASC4FIRST (Scemblix 1L PIII:see note) would drive use, helped by a better AE profile. Key hurdle likely to be reimbursement due to cost vs generics but noted this has been manageable for 2nd gen TKI's vs generic Gleevec.

Refer to important disclosures on page 3 to 5. **12646088**

Timestamp: 16 January 2024 12:30AM EST

Glossary

C3G = Complement 3 Glomerulopathy

C3GN = C3 Glomerulonephritis

DDD = Dense Deposit Disease

EGFR = Estimated Glomerular Filtration Rate

IC-MPGN = Immune-complex-mediated glomerulonephritis

PII / PIII = Phase 2 / 3

SGLT2 = Sodium-glucose co-transporter-2 inhibitor

ACE = Angiotensin converting enzyme

DKD = Diabetic Kidney Disease

APRIL = A Proliferation Inducing Ligand

1L/2L/3L = 1st Line / 3rd Line

CML = Chronic Myeloid Leukaemia

TKI = Tyrosine Kinase Inhibitor's

AE = Adverse Events

MMR = Major Molecular Response

HF = Heart Failure

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