Advagraf™ and the European Liver Transplant Registry (ELTR) data in liver transplantation

Media background

What is Advagraf™?

- Advagraf is an oral immunosuppressant licensed for the prevention of organ rejection in adult patients receiving liver and kidney transplants. It is a prolonged-release formulation of tacrolimus.

How does Advagraf work?

- When a person receives an organ from someone else during transplant surgery, their immune system may recognise the organ as foreign, and therefore the body will try to reject the new organ.
- Advagraf is used to reduce the strength of the body’s immune response, and lower the body’s ability to reject the transplanted organ.
- Tacrolimus, the active substance in Advagraf, is an immunosuppressant agent which acts on cells in the immune system (called T-cells) which are responsible for attacking the transplanted organ (organ rejection).

Who is Advagraf for?

- Liver failure occurs when large parts of the liver become damaged beyond repair and the liver is no longer able to function.
- Liver failure often occurs gradually and over many years.
  - Causes of liver failure include infections, reactions to prescription and herbal medications, chronic hepatitis with cirrhosis, Wilson’s disease, Hemochromatosis, alcoholism and liver cancer.
  - A liver transplantation is considered when the liver no longer functions adequately (liver failure).
- Nearly 6,000 liver transplantations are performed each year in Europe.
  - Liver transplantation offers patients with liver failure a second chance at life, but despite significant improvements in short-term outcomes,
around a quarter of patients will still die within five years of their transplantation

- Advagraf is indicated as prophylaxis of transplant rejection in adult kidney or liver allograft recipients
- Advagraf is indicated as a substitution for Prograf (tacrolimus twice daily) on the condition of a stable graft after kidney or liver transplantation

Non-adherence is commonly reported within patients who receive an organ transplant, reaching levels as high as 73% in liver transplant patients.

Compared to tacrolimus immediate release, Advagraf has been shown to improve patient adherence to treatment and has been shown to reduce high levels of variability in drug levels delivering a more consistent exposure.

**Advagraf: the ELTR study**

- The European Liver Transplant Registry (ELTR) represents 98% of overall European liver transplant data
- The ELTR collates data from 153 liver transplant centres in 27 European countries and is integral to improving best practice
- The aim of this ELTR study was to assess the effect of early use once-daily Advagraf versus tacrolimus immediate release (IR, twice daily) on long-term transplanted organ survival using real-world ELTR data as well as to assess the classical risk factors
  - The study was a retrospective analysis of 4,367 adult liver transplant patients receiving either Advagraf or tacrolimus IR, within the first month of transplantation and with a follow-up period of three years
  - Data was collated over a five year period (Jan 2008 – Dec 2012) from 21 centres that were using both formulations in patients surviving the first month post-transplant and the primary outcome measures were transplanted organ and patient survival rates
- Results of the study showed:
  - A significant graft survival benefit of 8% at 3 years (p=0.01) in liver transplant patients on Advagraf versus tacrolimus IR
  - An 8% organ survival advantage in the Advagraf arm versus tacrolimus IR, meaning the newly transplanted organs of patients treated with Advagraf were more likely to still be functioning three years post-

transplant compared with those treated with tacrolimus IR (88% vs 80%, p=0.01)\textsuperscript{15}.

- One graft loss was avoided for approximately every 13 patients treated with Advagraf within the first month post-transplantation\textsuperscript{165}.

- In addition in separate studies, compared to tacrolimus IR, Advagraf was shown to improve patient adherence to treatment\textsuperscript{8,9,10,11}.

- As with any registry based study, there are a number of limitations that must be considered when interpreting these data. Recognizing this issue the ELTR carried out additional analysis and when patients were matched for baseline characteristics, the significant long-term graft survival advantage with Advagraf was confirmed\textsuperscript{15}.

\*The differences in graft and patient survival rates for Advagraf and tacrolimus IR were assessed by Kaplan-Meier (KM) survival analysis\textsuperscript{15}.

References

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