

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

Media backgrounder

- Advagraf is a prolonged-release oral immunosuppressant¹

- Advagraf can minimise the chance of graft rejection¹

- There are several causes of liver failure

What is Advagraf™?

- Advagraf is an oral immunosuppressant licensed for the prevention of organ rejection in patients receiving liver and kidney transplants. It is a prolonged-release formulation of tacrolimus¹

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)¹

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 function²
- 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 cancer³
 - A liver transplant is considered when the liver no longer functions adequately (liver failure)³
- Nearly 6,000 liver transplants are performed each year in Europe.⁴
 - 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 transplant⁴

- Advagraf is indicated as prophylaxis of transplant rejection in adult kidney or liver allograft recipients⁵
- Advagraf can also be used to treat organ rejection in adult patients when other immunosuppressive medicines are not effective¹

Non-adherence is commonly reported within patients who receive an organ transplant, reaching levels as high as 73% in liver transplant patients.^{6,7}

Compared to tacrolimus immediate release, Advagraf has been shown to improve patient adherence to treatment.^{8,9,10,11} and has been shown to reduce high levels of variability in drug levels delivering a more consistent exposure.^{12,13}

Advagraf: the ELTR study

- The European Liver Transplant Registry (ELTR) represents 95% of overall European liver transplant data⁴
- The ELTR collates data from 145 liver transplant centres in 20 European countries and is integral to improving best practice⁴
- The aim of this ELTR study was to assess the effect of early use once-daily Advagraf versus tacrolimus immediate release (twice daily) on long-term transplanted organ survival using real-world ELTR data as well as to assess the classical risk factors⁶
 - 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 years⁶
 - 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 rates⁶
- 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^{14*}

• Liver transplantation offers patients with liver failure a second chance at life

• The ELTR represents 95% of overall European liver transplant data

• ELTR study found that Advagraf has a significant graft survival benefit compared to 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%, $p=0.01$)^{14*}
- One graft loss was avoided for approximately every 13 patients treated with Advagraf within the first month post-transplantation^{14*}
- In addition in separate studies, compared to tacrolimus IR, Advagraf was shown to improve patient adherence to treatment^{15,16,17,18}
- 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 confirmed⁶

*The differences in graft and patient survival rates for Advagraf and tacrolimus IR were assessed by Kaplan-Meier (KM) survival analysis⁶

References

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