Summary of Results for Laypersons

Astellas is grateful to the patients who took part in this clinical study. Thank you.

What was the Study Called?

A Phase IIIb Randomized Study of Intermittent Versus Continuous Androgen Deprivation Therapy Using ELIGARD® 22.5 mg 3-Month Depot in Subjects With Relapsing or Locally Advanced Prostate Cancer Who Are Responsive to Such Therapy. This is also known as the ICELAND study.

Why was this Study Needed?

Prostate cancer growth is dependent on male hormones or "androgens." An example of an androgen is testosterone. Eligard® (also known as leuprorelin acetate) is a prescription medicine for the treatment of prostate cancer. Eligard keeps the testicles from making testosterone by blocking other hormones that are needed to make it. This is called androgen deprivation therapy (or androgen deprivation for short). Androgen deprivation stops or slows down the growth of prostate cancer. It also lowers the serum level of a protein produced by prostate cancer cells. (Serum is the fluid part of blood.) That protein is called prostate-specific antigen (or PSA for short). Continuous androgen deprivation in men causes unwanted effects such as hot flashes, sweating, loss of sexual desire, impotence or the inability to have or maintain an erection during sexual intercourse, enlarged breasts and shrinking of the testicles. Some of the unwanted effects may happen less often with off-and-on (intermittent) androgen deprivation. Therefore, there was a need to study intermittent androgen deprivation for the treatment of prostate cancer.

This study was conducted in patients with prostate cancer. About half of the patients received continuous androgen deprivation with Eligard. The other half received intermittent androgen deprivation with Eligard. This study helped answer the question how the time to PSA progression compared between the 2 types of androgen deprivation. The time to PSA progression is the time from the start of study medicine until the time that the serum level of PSA rises to 4 ng/mL or more (4 ng or more of PSA in 1 mL of serum). The higher PSA serum level means that the prostate cancer got worse. And it means that the cancer is no longer controlled by the androgen deprivation. It was also important to find out what unwanted effects the patients had from the study medicine.

The study started in April 2006 and ended in April 2013. When the study ended, the sponsor of this study (Astellas) reviewed all the study information and created a report of the results. This is a summary of that report.

What Kind of Study was This and Who Took Part in it?

This was an "open-label" study. This means that each patient and the study doctors knew which dosing that patient received (continuous or intermittent androgen deprivation).

The study included men aged between 18 and 80 years. They had prostate cancer. Their cancer had spread from the prostate to nearby tissue or lymph nodes. Or their cancer had

come back after surgery to remove the entire prostate. Or it had come back after radiation treatment. Patients were active or they could perform light daily activities. Or they were able to walk and capable of all self-care, but unable to carry out any work activities. And they were up and about more than half of the time that they were awake. The patients were expected to live for at least 5 years.

During the study, the study doctor did a check-up of the patients at several study visits. At the first visit, patients were checked if they could be in the study. Patients who could be in the study received continuous androgen deprivation with Eligard for 6 months. This means that they received 2 injections, 3 months apart, of the 3-month form of Eligard beneath the skin. (The 3-month form releases medicine for 3 months.) Patients also took bicalutamide tablets (50 mg) by mouth once a day for the first month.

After 6 months, their serum level of PSA was checked ("6-month PSA check"). That level was measured on 2 occasions (at least 2 weeks apart) and could be no more than 1 ng/mL. Patients with the specified PSA level could remain in the study. They were picked for 1 of 2 treatments with study medicine (continuous or intermittent androgen deprivation) by chance alone.

- Continuous androgen deprivation: Patients received an Eligard 22.5 mg injection every 3 months.
- Intermittent androgen deprivation: Patients only received an Eligard 22.5 mg injection every 3 months after their serum levels of PSA rose to 2.5 ng/mL or more. Then, they also took bicalutamide tablets (50 mg) by mouth once a day for 1 month. If their PSA levels on 2 occasions (at least 2 weeks apart) dropped to 1 ng/mL or less, the Eligard injections were paused.

The patients received study medicine for up to 36 months (3 years).

This study took place at 102 clinics in several countries. 933 patients were in this study. After the 6-month PSA check, 701 patients could remain in the study. Out of these patients, 690 patients received at least 1 dose of study medicine and safety information was available for them.

	Number of Patients
Age Group	
Aged less than 65 years	100
Aged 65 years or older	590
Clinic Location	
European Union Countries (*at the time of this study*)	567
Belgium	19
Czech Republic	40
Denmark	6
Finland	17
France	60
Germany	138
Greece	16
Hungary	29
Ireland	3
Italy	35
The Netherlands	20
Poland	30
Portugal	18
Romania	6
Slovakia	47
Spain	65
Sweden	6
The UK	12
Outside European Union	123
Norway	16
Russia	107

What Were the Study Results?

This study in patients with prostate cancer helped answer the question how the time to PSA progression compared between continuous and intermittent androgen deprivation. The time to PSA progression is the time from the start of study medicine until the serum level of PSA rises to 4 ng/mL or more. This was measured on 3 successive occasions, with at least 2 weeks in between the measurements.

The time to PSA progression was similar with both types of androgen deprivation. PSA progression happened in 21 out of 352 patients (6.0%) who received continuous androgen deprivation. It happened in 20 out of 334 patients (6.0%) who received intermittent androgen deprivation. A statistical test showed that the difference between the 2 types of androgen deprivation was likely to be due to chance.

What Adverse Reactions did Patients Have?

A lot of research is needed to know whether a medicine causes a medical problem. So when new medicines are being studied researchers keep track of all medical problems that patients have while they are in the study. These medical problems are called “adverse events” and are recorded whether or not they might be caused by the treatment taken. An “adverse reaction”

is any medical problem or "adverse event" that is judged by the study doctor to be possibly caused by a medicine or treatment used in the study.

The table below shows the most common adverse reactions experienced by patients who received at least 1 dose of study medicine in this study.

Adverse Reaction	Continuous Androgen Deprivation (out of 353 patients)	Intermittent Androgen Deprivation (out of 337 patients)
Any adverse reaction	145 (41.1%)	124 (36.8%)
Feeling hot for a brief moment	66 (18.7%)	70 (20.8%)
Enlarged breasts in males	13 (3.7%)	11 (3.3%)
Constipation	11 (3.1%)	7 (2.1%)
Fatigue or tiredness	9 (2.5%)	8 (2.4%)
High blood pressure	9 (2.5%)	6 (1.8%)
Loss of sexual desire	9 (2.5%)	7 (2.1%)
Impotence or the inability to have or maintain an erection during sexual intercourse	7 (2.0%)	7 (2.1%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care.

Eight patients (1.2%, or 8 out of 690 patients) experienced serious adverse reactions in this study: 4 patients who received continuous androgen deprivation and 4 patients who received intermittent androgen deprivation.

36 patients died during the study. Six of the 36 patients died before the 6-month PSA-check and received continuous androgen deprivation and bicalutamide. The remaining 30 patients died after the 6-month PSA check: 10 patients who received continuous androgen deprivation and 20 patients who received intermittent androgen deprivation. None of the patients died because of the study medicine.

After the patients stopped receiving study medicine, the study doctor followed up with them for 18 months. The study doctor recorded any adverse events they had during that time. During that time, 60 patients died: 36 patients who had received continuous androgen deprivation and 24 patients who had received intermittent androgen deprivation. The causes of their deaths were unknown.

Where Can I Learn More About This Study?

This document is a short summary of the main results from this study and reflects the information available as of January 2014. You can find this summary and more information about this study online at http://www.astellasclinicalstudyresults.com.

Please remember that researchers look at the results of many studies to find out how well medicines work and which adverse reactions they might cause. This summary only shows

the results of this 1 study. Your doctor may help you understand more about the results of this study.

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