Summary of Results for Laypersons

What was the Study Called?

Randomized multicenter phase IV study to compare efficacy and safety of the two dosage regimens of nicardipine hydrochloride injection in hypertensive emergency patients

Why was this Study Needed?

Patients who have a hypertensive emergency have an extremely high blood pressure. Their top number (systolic blood pressure) is at least 180 millimeters of mercury (mmHg). Or their bottom number (diastolic blood pressure) is at least 120 mmHg. The high blood pressure damages their organs. This is a condition that can cause death. Nicardipine hydrochloride injection (also known as Perdipine Injection, Cardene I.V., Coponent, Isedipeal and Nisutadil) is a prescription medicine for the treatment of hypertensive emergency. It lowers the blood pressure. Nicardipine hydrochloride injection is given to patients as an intravenous infusion. For the infusion, a catheter (thin tube) is inserted into a vein of their arm. The allowed type of infusion rate differs by country.

Some countries (such as the US, Japan and countries in Europe) allow a set starting infusion rate, which is independent of the patient's body weight. The rate is then increased every 5 to 15 minutes until the desired blood pressure is reached. In other countries (such as China and South Korea), the infusion rate is based on body weight. The weight-based infusion rate is adjusted until the desired blood pressure is reached. In an emergency situation, it is difficult for doctors to calculate the infusion rate based on the patient's weight. The weight-independent infusion rate is easy and simple for doctors. This study helped answer the question if the weight-independent infusion rate decreased blood pressure the same as or better than the weight-based infusion rate. The study looked at the proportion of patients with hypertensive emergency who reached their desired blood pressure within 1 hour with each type of infusion rate. It was also important to find out what unwanted effects the patients had from each type of infusion rate.

This study for nicardipine hydrochloride injection took place at 9 clinics in China. The study took place from March 2013 to January 2014. When the study ended, the sponsor (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 the study doctor and the patients knew which type of infusion rate was used to administer nicardipine hydrochloride injection: weight-independent or weight-based.

Men and women could take part in the study if:

- They were at least 18 years of age.
- Their systolic blood pressure was at least 180 mmHg and/or their diastolic blood pressure was at least 120 mmHg. There was evidence that organs had been damaged

by the extremely high blood pressure. This included symptoms of sudden onset of chest pain due to not enough blood going to the heart; shortness of breath; feeling of discomfort in the abdomen (belly); fainting; dizziness (or sensation of lightheadedness, unsteadiness, or giddiness); blurred vision; confusion; blood in the urine; changes that result from not enough blood going to the heart and that show up in a test of the heart's electrical activity.

- They were able and willing to follow the study instructions.

Patients could not take part in the study if:

- Women were pregnant or breastfeeding.
- They were allergic to any component of the study medicine.
- They had a narrowed valve between the heart and the aorta. (The aorta is the main artery taking blood from the heart to the body.) This significantly restricted the blood flow from the heart to the aorta and the rest of the body.
- Their blood pressure increased before, during and/or after a surgical procedure.
- They had bleeding in the brain caused by abnormal connections of some of the blood vessels, an abnormal buildup of blood vessels and dead tissue in the brain resulting from a lack of blood flow. Or they had bleeding into the cavities in the brain, which produce and transport cerebrospinal fluid that protects the brain inside the skull. Or they had brain damage that was caused by a blow to the head or the body and that resulted in bleeding in the brain.
- The study doctor checked the patients. The study doctor then decided that it would not be safe for the patients to take part in the study. Or that it could be difficult to interpret the study results if the patients took part in the study.

The study doctor determined the desired blood pressure for each patient who could be in the study. The desired blood pressure was based on the patient's medical condition. The desired systolic blood pressure was 160 mmHg or lower. But a result between 155 and 165 mmHg was acceptable. The desired diastolic blood pressure was 100 mmHg or lower. But a result between 95 and 105 mmHg was acceptable. All patients received nicardipine hydrochloride as an intravenous infusion. The patients were picked by chance alone for 1 of the types of infusion rates:

- Weight-based infusion rate: The infusion rate was between 0.5 and 6 μg per minute per kg of body weight. The study doctor usually started with a low infusion rate. The study doctor gradually increased the rate until he or she reached the desired blood pressure.
- Weight-independent infusion rate: The starting infusion rate was 5 mg per hour. Every 5 to 15 minutes, the study doctor increased the rate by 2.5 mg per hour until he or she reached the desired blood pressure. The maximum allowed rate was 15 mg per hour.

The study doctor checked on the patients from the start of the infusion until 48 hours thereafter or until they left the clinic. Patients' blood pressure and heart rate were measured often during that period. At first, blood pressure and heart rate were measured every 5 to

15 minutes. This was done from the start of the infusion until 1 hour thereafter or until the desired blood pressure was reached (whichever came later). Blood pressure and heart rate were then measured every 15 minutes or as often as needed based on the patient's symptoms. This was done until 2 hours after the start of the infusion.

A total of 163 patients were in the study. A total of 160 patients received at least 1 dose of study medicine as an intravenous infusion.

- 80 patients received study medicine at an infusion rate that was weight-based.
- 80 patients received study medicine at an infusion rate that was weight-independent.

	Number of Patients	
	Weight-based Infusion Rate	**Weight-independent Infusion Rate**
Age Group		
Aged 23 to 94 years	80	80
Sex		
Men	35	37
Women	45	43
Clinic Location		
European Union Countries	0	0
Outside European Union	80	80
China	80	80

What Were the Study Results?

This study was conducted in patients with a hypertensive emergency. All patients received nicardipine hydrochloride injection as an intravenous infusion. An infusion rate based on body weight was used to give study medicine to half of the patients. A weight-independent infusion rate was used to give study medicine to the other half. This study tested if the weight-independent infusion rate decreased blood pressure the same as or better than the weight-based infusion rate. The study looked at the proportion of patients who reached their desired blood pressure within 1 hour with each type of infusion rate.

The study showed that when the weight-based infusion rate was used, 68 out of 80 patients (85.0%) reached their desired blood pressure within 1 hour. 74 out of 80 patients (92.5%) did so when the weight-independent infusion rate was used. The study showed that the weight-independent infusion rate was as good as the weight-based infusion rate in decreasing blood pressure.

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 adverse reactions experienced by patients who received at least 1 dose of study medicine while taking part in this study.

There was no difference in adverse reactions between the 2 types of infusion rates.

Adverse Reaction	Weight-based Infusion Rate (out of 80 patients)	Weight-independent Infusion Rate (out of 80 patients)
Increased heart rate	1 (1.3%)	1 (1.3%)
Increased blood level of a liver enzyme (alanine aminotransferase)	1 (1.3%)	1 (1.3%)

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

None of the patients experienced a serious adverse reaction.

Where Can I Learn More About This Study?

After evaluating the results of this clinical study Astellas may perform additional studies to better understand nicardipine hydrochloride injection.

This summary of the clinical study results is available 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. If you have questions about nicardipine hydrochloride injection, please discuss these with your doctor.

Sponsors contact details:

Astellas Pharma China, Inc.
19th Floor, 1901-1904, SK
Capital Tower Beijing
No 6, Jia Jianguomenwai Avenue
Chaoyang District
Beijing, 100022
China