

A Large, Vertically Integrated Health Systems Parallel *Process Initiative*¹

Expediting the Process of Evaluating and Treating Stroke

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***Genentech evaluated a parallel process initiative in a large, vertically integrated health system to highlight an example of process improvement in patient management.**

Indication

Activase® (alteplase) is indicated for the treatment of acute ischemic stroke (AIS). Exclude intracranial hemorrhage as the primary cause of stroke signs and symptoms prior to initiation of treatment. Initiate treatment as soon as possible but within 3 hours after symptom onset.

Important Safety Information

Contraindications

Do not administer Activase to treat acute ischemic stroke in the following situations in which the risk of bleeding is greater than the potential benefit: current intracranial hemorrhage (ICH); subarachnoid hemorrhage; active internal bleeding; recent (within 3 months) intracranial or intraspinal surgery or serious head trauma; presence of intracranial conditions that may increase the risk of bleeding; bleeding diathesis; and current severe uncontrolled hypertension.

Please see Important Safety Information throughout and full [Prescribing Information](#).

A LARGE, VERTICALLY INTEGRATED HEALTH SYSTEMS PARALLEL PROCESS INITIATIVE¹

Expediting the Process of Evaluating and Treating Stroke

Overview of the Acute Stroke Redesign Process

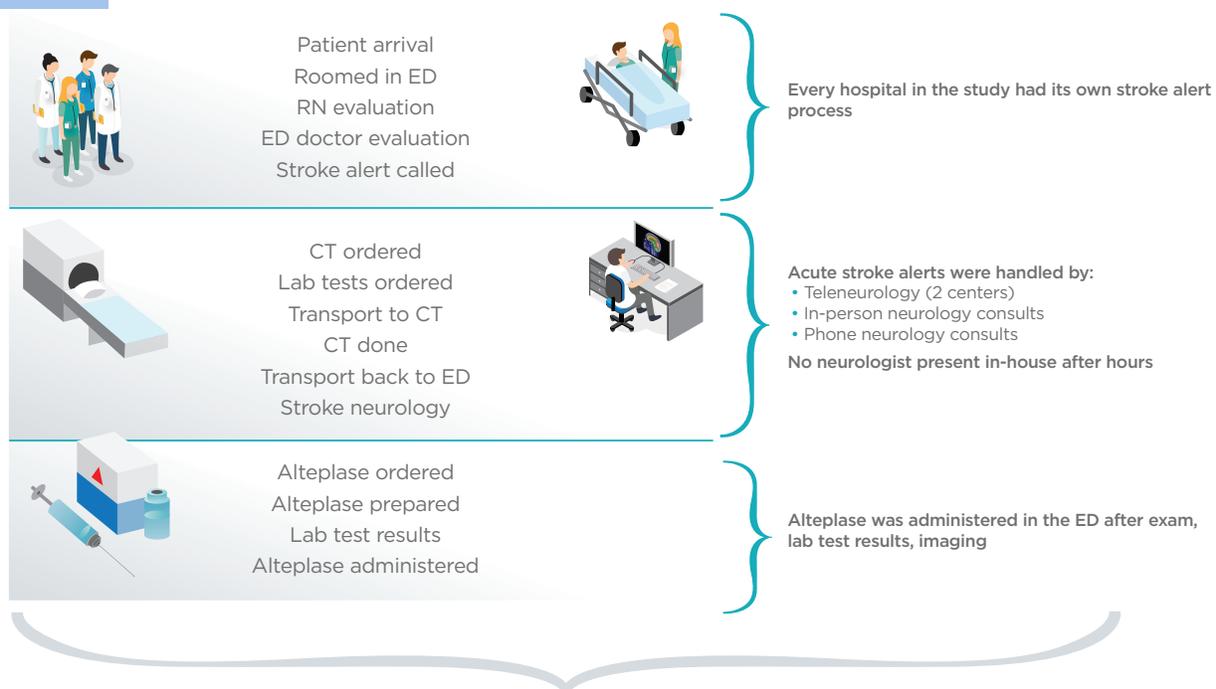
The *Process Initiative* was established due to a recognized need to evaluate and attend to stroke patients more quickly. Its goal was to evaluate the acute stroke process and identify opportunities for improvement. Several factors were taken into account, including:

- Geography – 21 medical centers spread over 17,000 square miles
- Inconsistency among hospitals – each had its own stroke alert process and widely variable door-to-needle (DTN) time

Stroke Process Approach Prior to the *Process Initiative*

Prior to the *Process Initiative*, stroke care employed a serial, or sequential method: each task was accomplished one after the other, in a step-by-step manner (Figure 1). Under this approach, alteplase was administered in the emergency department (ED), after exams, lab test results, and imaging. Although a DTN time of 60 minutes was achieved 60% of the time, DTN time was variable across medical centers.

Figure 1.



Variable baseline DTN time among hospitals

CT, computed tomography; DTN, door-to-needle; ED, emergency department

Important Safety Information Warnings and Precautions

Bleeding

Activase can cause significant, sometimes fatal, internal or external bleeding, especially at arterial and venous puncture sites. Avoid intramuscular injections and trauma to the patient. Fatal cases of hemorrhage associated with traumatic intubation in patients administered Activase have been reported. The concomitant administration of heparin and aspirin with and following infusions of Activase for the treatment of AIS during the first 24 hours after symptom onset has not been investigated. Because heparin, aspirin, or Activase may cause bleeding complications, carefully monitor for bleeding, especially at arterial puncture sites. Hemorrhage can occur 1 or more days after administration of Activase, while patients are still receiving anticoagulant therapy. If serious bleeding occurs, terminate the Activase infusion.

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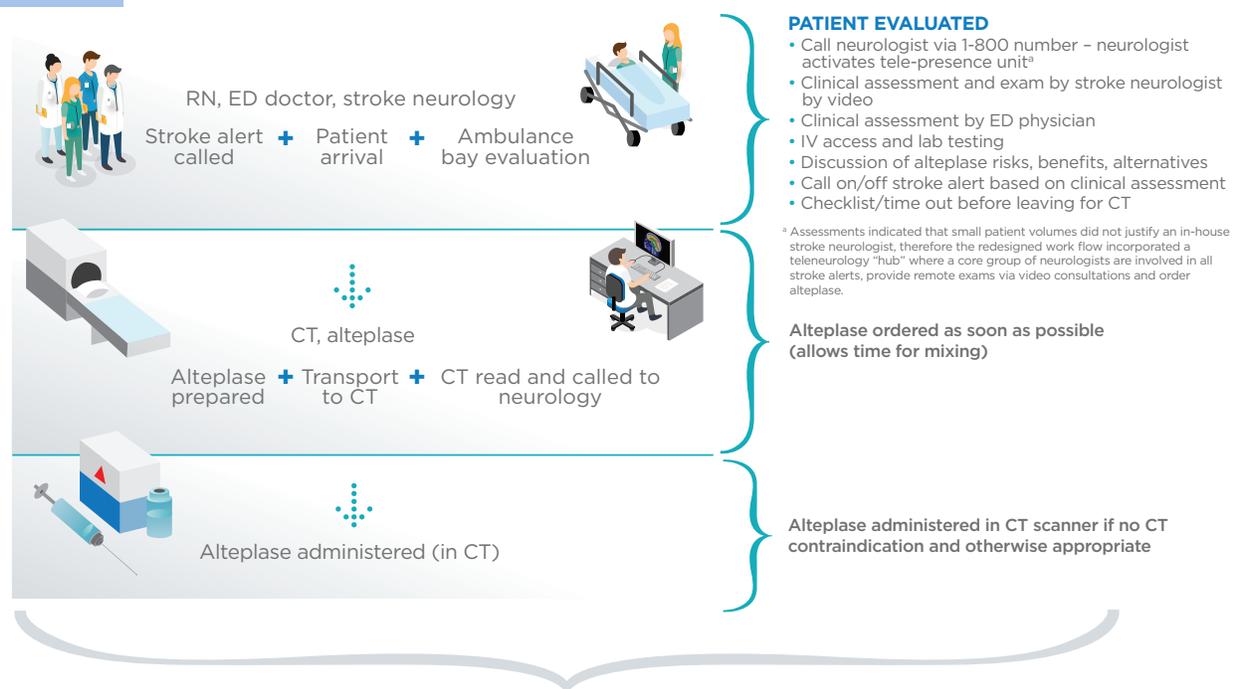
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The Parallel Path Approach After the *Process Initiative*

The *Process Initiative* set out to examine what would be required to achieve “world class” DTN times of 15-20 minutes. Among the goals identified for its regional stroke program were expeditious patient evaluation and determination of alteplase eligibility, as well as efficient alteplase treatment. Key components to speed were recognized and a new parallel stroke process, in which steps occurred concurrently, was implemented (Figure 2). Once this strategy was employed, patients were no longer roomed in the ED and went straight for a CT scan, where they also were administered alteplase, as appropriate.

Figure 2.



Improved DTN time among hospitals

CT, computed tomography; ED, emergency department; IV, intravenous

Important Safety Information Warnings and Precautions

Bleeding (cont'd)

In the following conditions, the risks of bleeding with Activase are increased and should be weighed against the anticipated benefits: recent major surgery or procedure; cerebrovascular disease; recent intracranial hemorrhage; recent gastrointestinal or genitourinary bleeding; recent trauma; hypertension; high likelihood of left heart thrombus; acute pericarditis; subacute bacterial endocarditis; hemostatic defects including those secondary to severe hepatic or renal disease; significant hepatic dysfunction; pregnancy; diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions; septic thrombophlebitis or occluded AV cannula at seriously infected site; advanced age; and patients currently receiving oral anticoagulants, or any other condition in which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location.

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Expediting the Process of Evaluating and Treating Stroke

Key Findings and Process Outcomes

After standardizing stroke treatment procedures, the *Process Initiative* successfully increased the number of patients receiving alteplase and decreased DTN times. Comparing the periods before (1/1/15–9/15/15; Figure 3A) and after (9/16/15–1/31/16; Figure 3B) the *Process Initiative* at all 21 sites:

- The median DTN time decreased from 53 to 39.8 minutes
- The rate of DTN <30 minutes increased from 5% to 28.9%
- The number of eligible patients receiving alteplase/month increased from 51.3 to 70.7

Figure 3A.

Alteplase cases and door-to-needle (DTN) time for all 21 stroke centers before the *Process Initiative* (01/01/2015–09/15/2015)

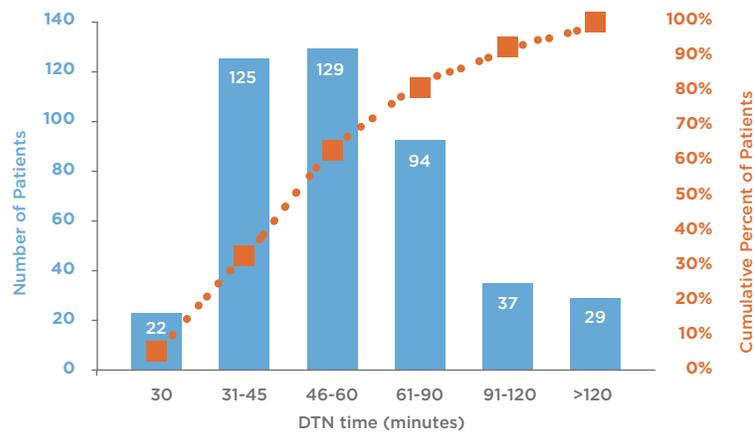
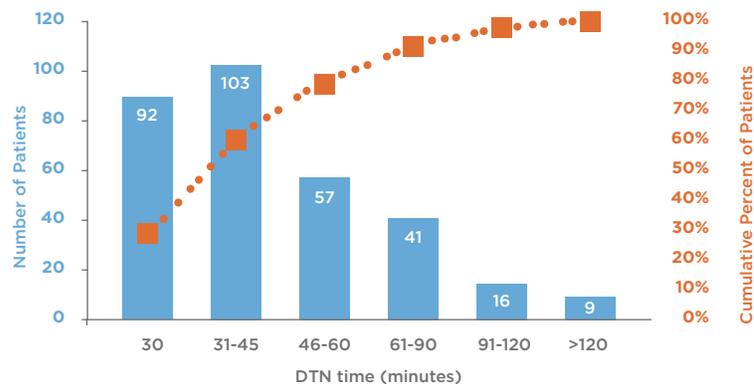


Figure 3B.

Alteplase cases and door-to-needle (DTN) time for all 21 stroke centers after the *Process Initiative* (09/16/2015–01/31/2016)



Important Safety Information

Orolingual Angioedema

Orolingual angioedema has been observed during and up to 2 hours after infusion in patients treated for AIS. In many cases, patients received concomitant angiotensin-converting enzyme inhibitors. Monitor patients treated with Activase during and for several hours after Activase infusion for orolingual angioedema. If angioedema develops, discontinue the Activase infusion and promptly institute appropriate therapy.

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Reference: 1. Nguyen-Huynh MN, Klingman K. KPNC stroke EXPRESS expediting the process of evaluating and stopping stroke. Presentation at: International Stroke Awareness Conference; February 17, 2016; Los Angeles, CA.

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Cholesterol Embolization

Cholesterol embolism, sometimes fatal, has been reported rarely in patients treated with thrombolytic agents; the true incidence is unknown. It is associated with invasive vascular procedures and/or anticoagulant therapy.

Coagulation Tests May be Unreliable during Activase Therapy

Coagulation tests and/or measures of fibrinolytic activity may be unreliable during Activase therapy unless specific precautions are taken to prevent in vitro artifacts.

Adverse Reactions

The most frequent adverse reaction associated with Activase AIS therapy is bleeding.

Although exploratory analyses of the AIS clinical studies suggest that severe neurological deficit (National Institutes of Health Stroke Scale [NIHSS] > 22) at presentation was associated with an increased risk of intracranial hemorrhage, efficacy results suggest a reduced but still favorable clinical outcome for these patients.

Allergic-type reactions, e.g., anaphylactoid reaction, laryngeal edema, orolingual angioedema, rash, and urticaria have been reported.