Gennova Biopharmaceuticals

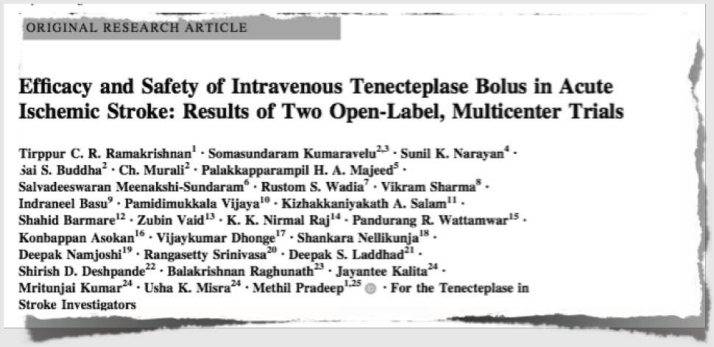
Neurology

Tenecteplase

TENECTASE®

Indicated in thrombolytic treatment of acute ischemic stroke within three hours of stroke initiation.

Published efficacy and safety



ORIGINAL RESEARCH ARTICLE

Efficacy and Safety of Intravenous Tenecteplase Bolus in Acute Ischemic Stroke: Results of Two Open-Label, Multicenter Trials

Tirppur C. R. Ramakrishnan[1] · Somasundaram Kumaravelu[2,3] · Sunil K. Narayan[4] · Jai S. Buddha[2] · Ch. Murali[2] · Palakkapparampil H. A. Majeed[5] · Salvadeeswaran Meenakshi-Sundaram[6] · Rustom S. Wadia[7] · Vikram Sharma[8] · Indraneel Basu[9] · Pamidimukkala Vijaya[10] · Kizhakkaniyakath A. Salam[11] · Shahid Barmare[12] · Zubin Vaid[13] · K. K. Nirmal Raj[14] · Pandurang R. Wattamwar[15] · Konbappan Asokan[16] · Vijaykumar Dhonge[17] · Shankara Nellikunja[18] · Deepak Namjoshi[19] · Rangasetty Srinivasa[20] · Deepak S. Laddhad[21] · Shirish D. Deshpande[22] · Balakrishnan Raghunath[23] · Jayantee Kalita[24] · Mritunjai Kumar[24] · Usha K. Misra[24] · Methil Pradeep[1,25] · For the Tenecteplase in Stroke Investigators

The study concludes that intravenous TNK-tPA given within 3 hours of symptom onset, is a safe, efficacious and well tolerated option in patients with acute ischemic stroke.

Comparison of results of pooled data with NINDS trial

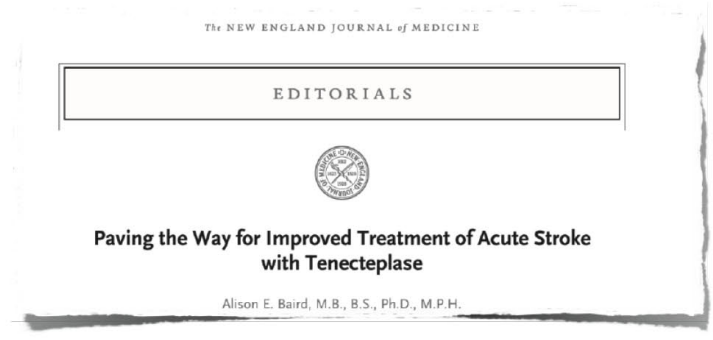
Outcome	TNK-tPA Study 0.2 mg/kg (N=91)	NINDS Study rt-PA* (N=144, Part I; N=168, Part II)	p value
Primary outcome, MNI	20 (22)	NA	-
Primary outcome modified for comparison with NINDS trial, NIHSS improvement by ≥ 4 points or a score of 0 at 24 h	53 (58.2)	67 (47)	0.083
Secondary outcomes			
mRS Score (at 3 months)			
0 or 1	64 (70.3)	66 (39)	< 0.001
2 or 3	13 (14.3)	35 (21)	0.24
4 or 5	9 (9.9)	39 (23)	0.01
BI Score (at 3 months)			
95-100	46 (50.5)	84 (50)	1.0
50-90	33 (36.3)	27 (16)	< 0.001
Symptomatic ICH	1 (1.1)	20 (6.4)	0.05
Mortality	5 (5.5)	28 (17)	0.01

TNK-tPA study data includes patients from study-I (30 patients) and study-II (61 patients) that were administered 0.2 mg/kg TNK-tPA. Data are expressed as N (%).

BI Barthel Index, *ICH* intracranial hemorrhage, *MNI* major neurological improvement, *mRS* modified Rankin Scale, *NA* data not available, *NIHSS* National Institutes of Health Stroke Scale, *NINDS* National Institute of Neurological Disorders and Stroke, *rt-PA* alteplase, *TNK-tPA* tenecteplase.

*For the NINDS study values, the mRS and BI from part 2, NIHSS improvement from part 1 and sICH from part 1 and part 2 are shown as these were treated as the primary end points in the trial (NINDS rt-PA Stroke Study Group New Engl J Med 1995). MNI is defined as improvement of ≥ 8 points or a score of 0 on NIHSS at 24 h. NA indicates data not available.

Global Perspective :

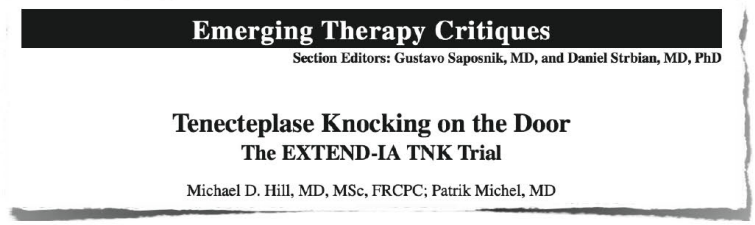


The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Paving the Way for Improved Treatment of Acute Stroke with Tenecteplase

Alison E. Baird, M.B., B.S., Ph.D., M.P.H.



Emerging Therapy Critiques

Section Editors: Gustavo Saposnik, MD, and Daniel Strbian, MD, PhD

Tenecteplase Knocking on the Door
The EXTEND-IA TNK Trial

Michael D. Hill, MD, MSc, FRCPC; Patrik Michel, MD

TENECTASE® is approved for Acute Ischemic Stroke

We have affordable solution for :

- ~3800 new cases of ischemic stroke every day in India
- 6.2 million deaths globally due to stroke
- About 85% of global stroke mortality which occurs in low and middle income countries

3rd Generation Thrombolytic

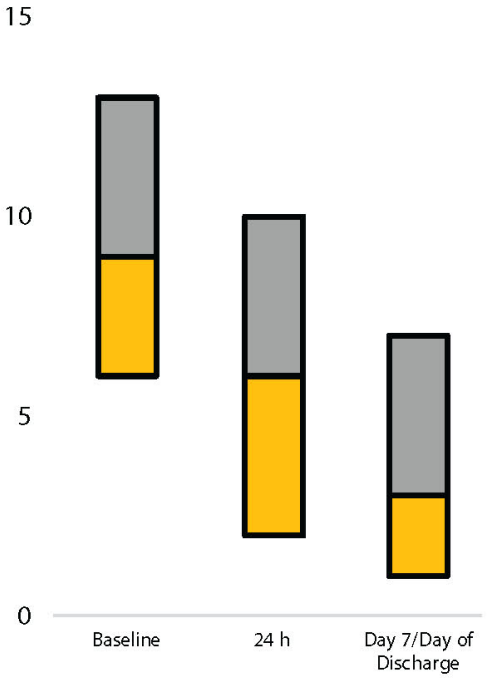
- Administered as a single bolus
- Dose: 0.2 mg/kg body weight
- Longer half life of 18-22 min
- 14 fold greater fibrin specificity than alteplase
- 80 times lesser susceptibility to PAI-1 than alteplase

Aim: To evaluate whether routine use of TNK-tPA within 3 hours after onset of stroke symptoms is
(a) safe (primary endpoint) and
(b) beneficial
(secondary endpoint)

IRIS-TNK (Indian Registry in Ischemic Stroke-Tenecteplase)

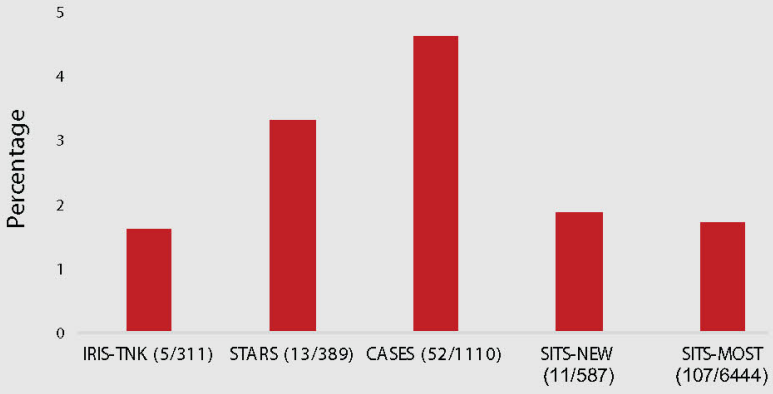
- Open-label, Prospective, Multicenter, Non Randomized, Ongoing, Observational study
- Patients (satisfying the eligibility criteria), would be followed up for three months post thrombolysis
- **Primary safety outcome variable:** Symptomatic ICH within 36±6 h after start of thrombolysis treatment
- **Secondary efficacy outcome variable:** NIHSS improvement ≥4 points or 0 at 24 h, 7 days (or day of discharge) post treatment initiation
- Modified Rankin Scale (mRS) Score 0-2 at three months (Functional Independence)
- mRS 0-1 at three months (Excellent Outcome)

NIHSS score



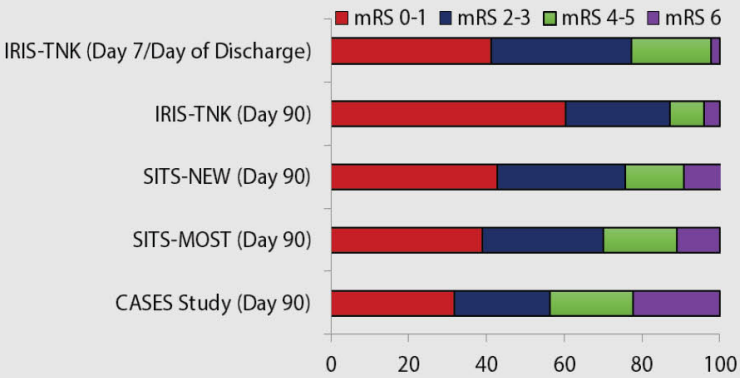
Median (Interquartile Range, 25th-75th Percentile)
Horizontal Line inside the box indicates median

Symptomatic ICH



SITS-NEW (Alteplase, Asia)
SITS-MOST (Alteplase, Europe)
CASES Study (Alteplase, Canada)
STARS Study (Alteplase, USA)

Excellent Outcome: mRS 0-1



Global patent for the indication

PATENT OFFICE
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GOVERNMENT OF INDIA

INTELLECTUAL PROPERTY INDIA

To
CHITRA ARVINDRAJESHWARI &
ASSOCIATES,AMSOFT BUSINESS CENTRE,UNITECH
TRADE CENTRE,SECTOR 43, GORGAON - 122
002,HARYANA, INDIA

Date of Dispatch 23 May 2017

Sub : Patent No.283474 (3516/MUM/2010), Dated 23/12/2010 (Ante-Dated :)Granted On Dated 23/05/2017

This is to state that a patent has been granted on the above-mentioned application and that the grant ofthe patent has been recorded in the Register of Patents on the 23/05/2017. The said patent is enclosedherewith.

The payment of renewal fee is required to be made at this office within three(3) months from the aforesaiddate of recording according to the proviso in sub-section(4) of Section 142 of the Patents Act,1970, asAmended by the Patent(Amendment)Act,2005/ Patent Rule, 2003 as Amended by Patent(Amendment)Rules,2006.

The renewal fee schedule has been given at the back of the Letter of Patent

Encl: As above

Nanavath Ramchander

DEPUTY CONTROLLER of of Patents & Designs

Country	Patent Number	Year Granted
India	283474	2017
USA	US9943575 B2	2018
Europe	EP2654770 B1	2017
Eurasia	026017	2017
Japan	6375112	2018
Australia	2011346515	2017
Mexico	356199	2018
New Zealand	611706	2015
Malaysia	Under Examination	
Columbia	Under Examination	
Brazil	Under Examination	
Indonesia	Under Examination	
UAE	Under Examination	

The United States of America

The Director of the United States Patent and Trademark Office

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America, and if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States of America, or importing into the United States of America, products made by that process, for the term set forth in 35 U.S.C. 154(a)(2) or (c)(1), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b). See the Maintenance Fee Notice on the inside of the cover.

Gennova Biopharmaceuticals Ltd., headquartered in Pune, India, is a biotechnology company dedicated to the development, production and commercialization of bio-therapeutics to address life-threatening diseases across various indications. Incorporating recombinant DNA technologies together with innovative bio-manufacturing practices, Gennova has created cost effective solutions for manufacturing and successfully commercializing bio-therapeutics across cardiovascular, neurology, nephrology and oncology markets.

Gennova Biopharmaceuticals

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