Stroke Update 2024

S.H. Reza Salari Namin
M.D
Stroke Neurologist

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Hamid R. Salari-Namin, M.D.

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I DO NOT have a financial relationship with an ineligible company.

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Learning Objectives

Title: Stroke Update 2024

Speaker: Hamid R. Salari-Namin, M.D.

Learning Objectives:

1. Explain the difference in uses of TNK vs TPA
2. List new recommendations for endovascular thrombectomy
3. Describe the therapeutic role of platelet antagonists-antithrombotic
4. Explain the role of antithrombotic vs thrombolysis in small strokes
5. Implement secondary stroke prevention

Overview

1. Thrombolytics
2. EVT in Anterior Circulation Stroke
3. EVT in Posterior Circulation Stroke
4. AIS secondary to intracranial atherosclerotic disease (ICAD)
5. Stroke with Atrial Fibrillation (AF)

Thrombolytics: IV TPA (Altepase)

- IV-TPA (1995 –NINDS*): Within 3 hrs. of symptom onset
- IV-TPA (2008 –ECASSIII*): Extended to 4.5 hrs.
- IV-TPA (2021-EXTEND*): No benefit beyond 4.5-9 hrs.
- IV-TPA (2018 MR WITNESS*/2018 WAKE UP*): In acute ischemic stroke (AIS) of unknown onset (14% - 27% of strokes) treatment group achieved 11.7% better 90-day outcomes (*P=0.02)

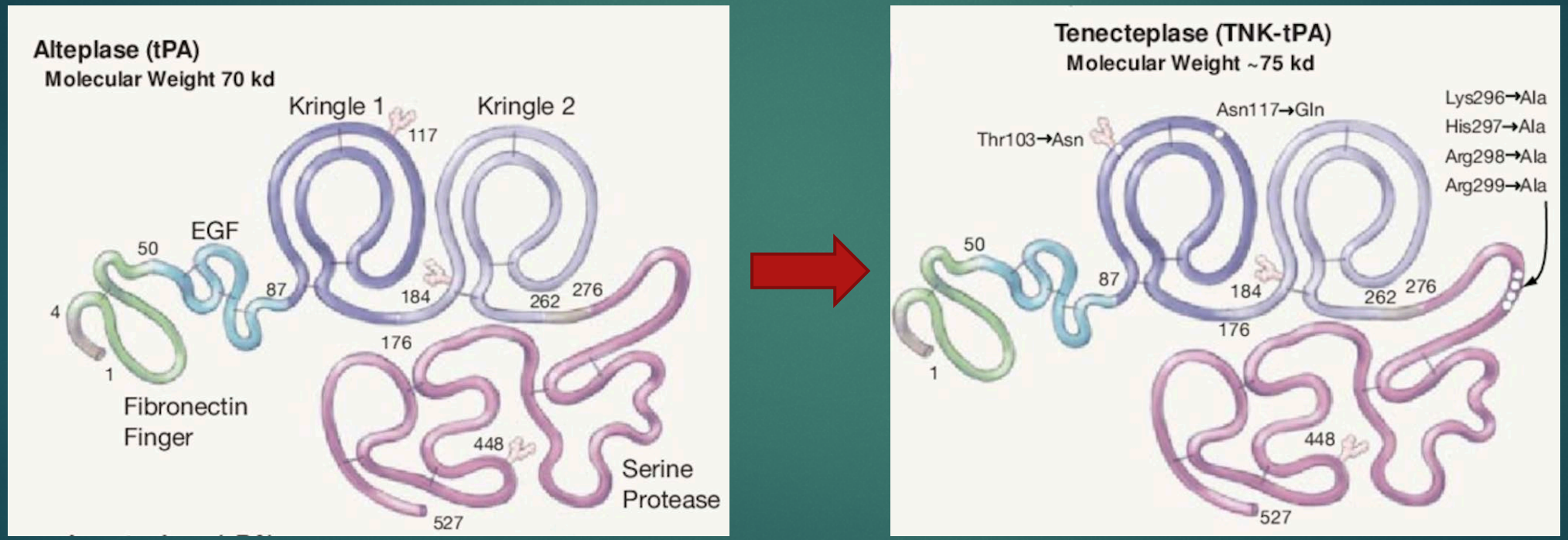
Thrombolytics: IV TNK (Tenecteplase)

- Genetically engineered alteplase – 3 point mutations result in:
  - Increased fibrin affinity/specificity
  - Increased resistance to PAI-1
  - Longer half life (90-130 min.)
- Dosage: 0.25mg/kg (max 25mg), single IV bolus over 5-10 sec.
  - No dose adjustment for renal/hepatic impairment

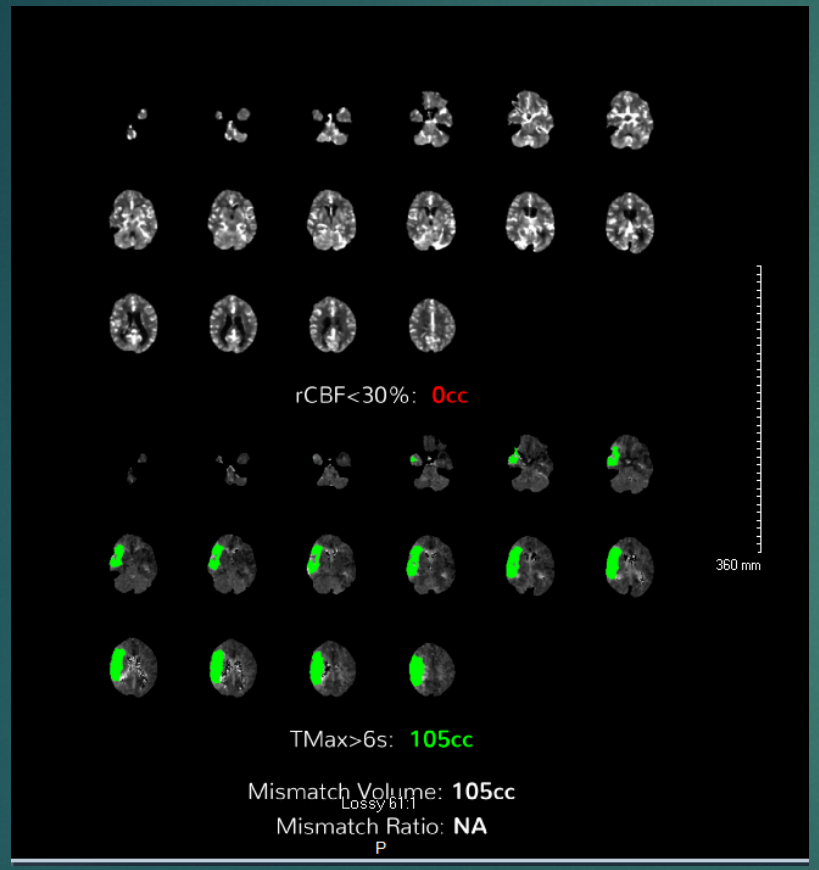
- IV TNK (2018 - EXTEND-IA TNK *): Administration before Endovascular Therapy (EVT) resulted in improved revascularization and 90-day outcomes compared to IV-TPA

- IV TNK (2023 -TRACE-2/2022 AcT *): Noninferior to TPA in patients presents within 4.5 hrs. of AIS

Altepase vs. Tenecteplase: Molecular Comparison



Case Study 1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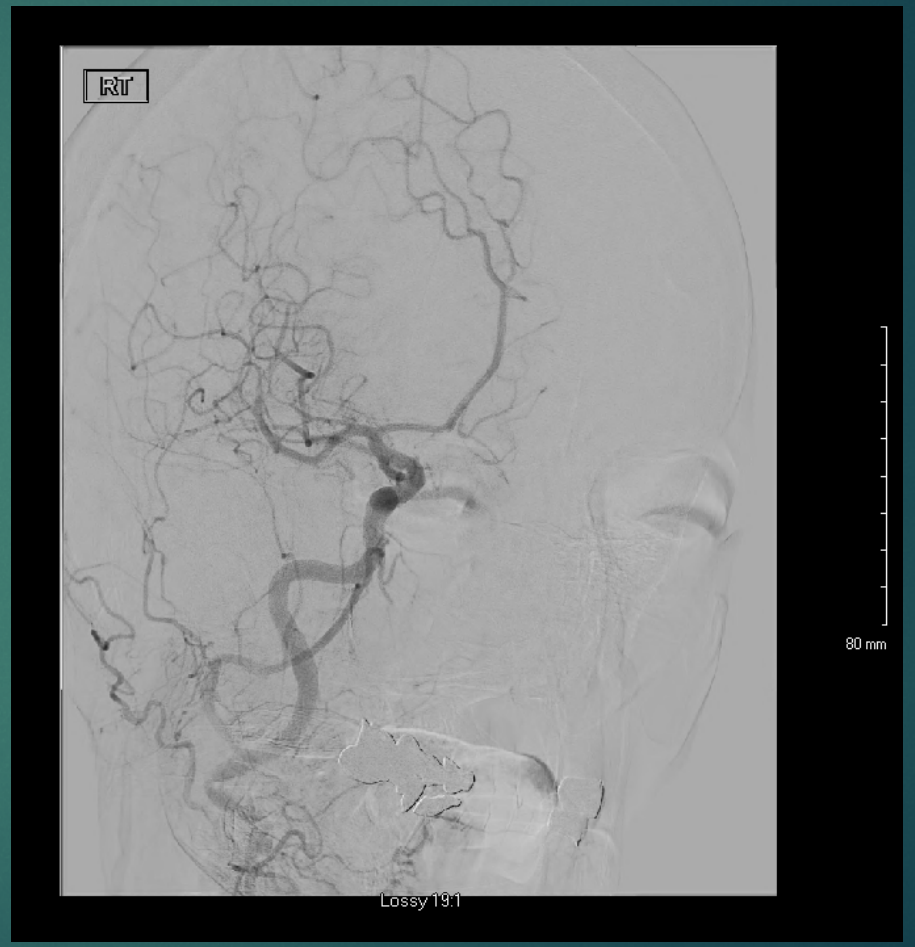
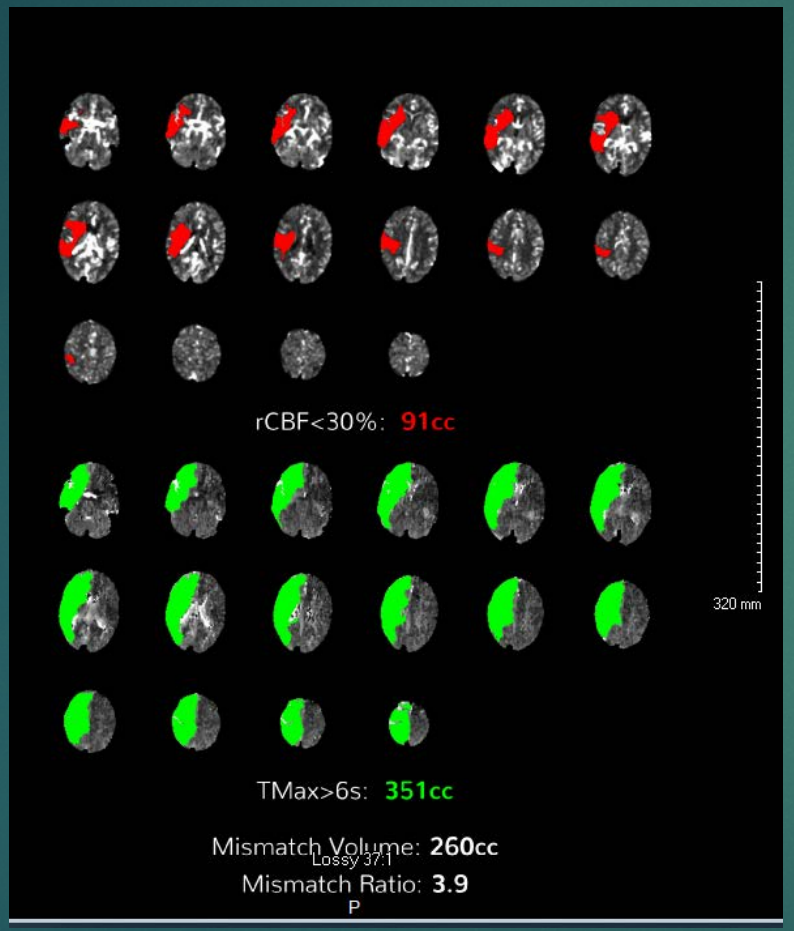
Case Study 1



Case Study 2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Mismatch Ratio: 3.9
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Lossy 10:1

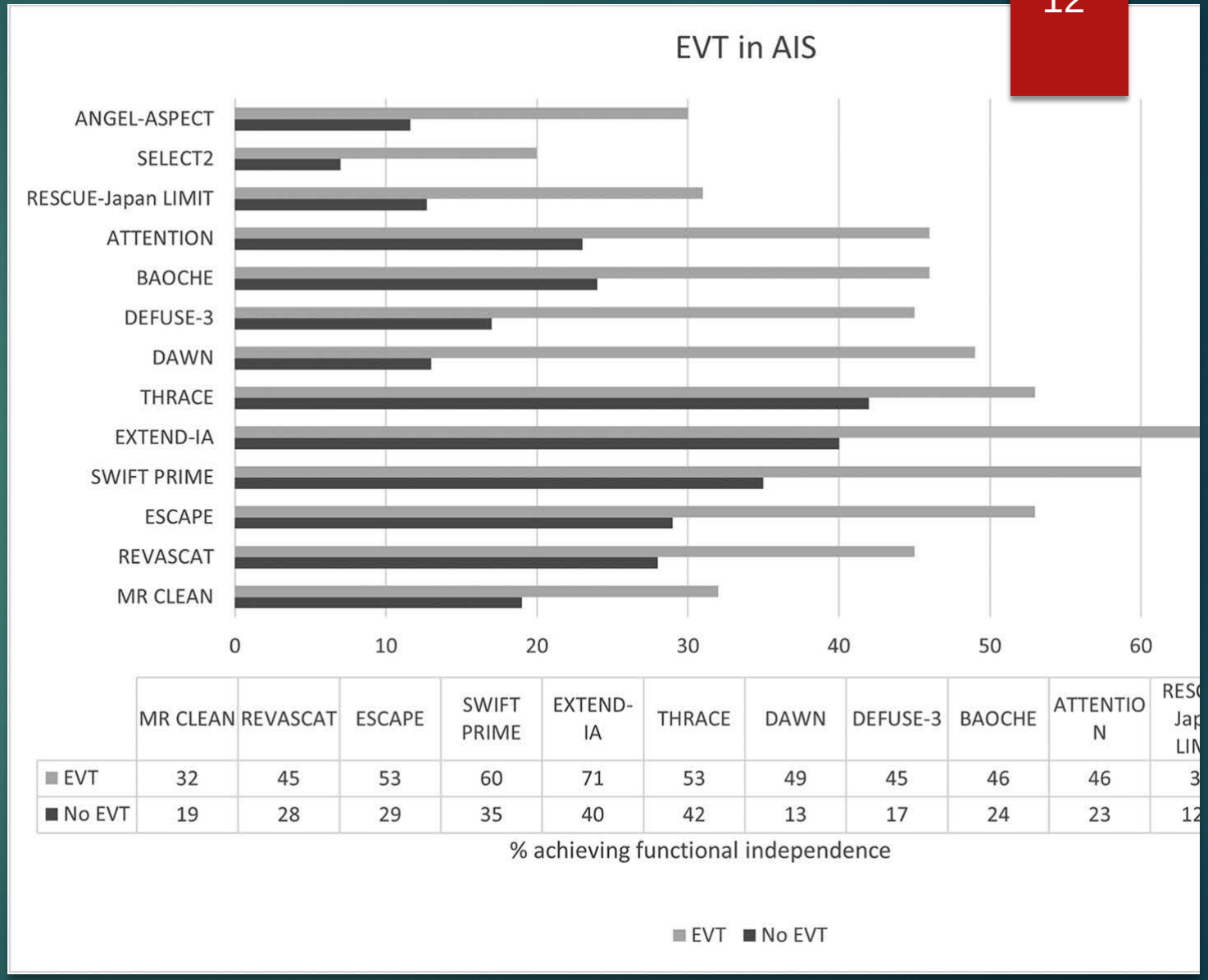
Case Study 2

Case Study 3

Case Study 3

EVT in anterior circulation stroke

- 5 RCTs (2015) showed efficacy of EVT over standard medical management in patients with anterior circulation stroke with proximal LVO
  - MR CLEAN *
  - SWIFT PRIME *
  - EXTEND-IA *
  - REVASCAT *
  - THRACE *



	MR CLEAN	REVASCAT	ESCAPE	SWIFT PRIME	EXTEND-IA	THRACE	DAWN	DEFUSE-3	BAOCHE	ATTENTION	RESCUE-Japan LIMIT
EVT	32	45	53	60	71	53	49	45	46	46	3
No EVT	19	28	29	35	40	42	13	17	24	23	12

EVT in anterior circulation stroke

- Metanalysis of 5 major EVT trials (2016 - HERMES*) found:
  - Effectiveness of EVT declined w/ each passing hr.
  - Treatment within first 7 hours is likely to produce best result
  - # needed to treat: 2.6

EVT in anterior circulation stroke

- Effectiveness of EVT in delayed time windows (up to 24 hrs.)
  - 2017 - DAWN* (6-24 hrs.) : Increased functional independence in patients who had clinical/imaging mismatch
  - 2018 - DEFUSE 3* (6-16 hrs.) : Improved outcome in patients who met certain imaging criteria (ACS with LVO involving ICA or proximal MCA, core infarct of <70mL, ischemic tissue to infarct ratio > 1.8)

EVT in anterior circulation stroke

- Combined IV-TPA and EVT compared with EVT alone:
  - 2020-DIRECT-MT* / 2021-DEVT* : EVT alone non-inferior to combined therapy
  - 2021- MR-CLEAN No. IV* : EVT was neither superior nor non-inferior to combined therapy
  - 2021-DIRECT-SAFE* : EVT non-inferior to combined therapy
    - Asian pts. did better with combined therapy

EVT in large core infarcts

- Large core infarcts (ASPECT < 5 OR core infarct < 70mL) excluded in trials secondary to poor outcome
- 2022-RESCUE-Japan LIMIT* :
  - Prospective RCT, pts with large infarct core (ASPECTS 3-5)
  - → Improved functional outcome (9-day mRS 0-3) in pts who received EVT compared with SMM
- 2023-SELECT 2* and ANGEL-ASPECT** :
  - Pts with large infarct core (*core >= 50mL, **ASPECTS 3-5 AND 70-100 mL)
  - → BOTH trials stopped early due to **overwhelmingly** improved outcomes with EVT

EVT in Tandem Lesions

- Tandem lesions: Anterior circulation LVOs with concurrent high-grade stenosis OR occlusion of the ipsilateral ICA
- Optimal management remains unclear:
  - 2022-ESCAPE-NA 1* → concurrent tandem lesion DID NOT lower odds of good functional outcome, regardless of stent placement

EVT in posterior circulation stroke (PCS)

- Posterior circulation LVOs → 7-12% of intracranial LVOs in AIS
- 4 RCTs evaluated role of EVT in PCS
  - 2020-BEST *
  - 2021- BASICS *
  - 2022- BAOCHE *
  - 2022- ATTENTION *
  - → Improvement of outcomes in PCS presenting between 6-24 hrs. AND <12 hrs. of last well known

AIS secondary to intracranial atherosclerotic disease (ICAD)

- ICAD 10-15% of AIS cases in West, BUT higher prevalence in Asia
- Higher risk of recurrent stroke AND acute vessel re-occlusion despite recanalization during EVT
- 2011-SAMMPRIS*: Terminated early due to significantly higher complication rate in stented group
- 2015-VISSIT*: Terminated early due due to increased stroke risk with stent placement
- 2022-CASSISS*: No additional benefit of stent placement over SMM
- 2023-WICAD*: Excellent safety profile when used by experienced interventionalists. Functional independence (mRS 0-2) was achieved in 88.9% of pts. with 3% mortality rate

Stroke with Atrial Fibrillation (AF)

2023 – Circulation ACC/AHA Guideline for the diagnosis and management of AF*

- Implantable monitors useful in patients with stroke and suspicion of underlying AF
- AF pattern is less important than stroke risk in deciding about treatment
- Direct Oral Anti-Coagulant Agents (DOACs) are preferred for stroke prevention in patients with AF
- Bridging anticoagulation if DOACs need to be interrupted in patients needing surgery/procedures is **not** recommended

Stroke with Atrial Fibrillation (AF)

2023 – Early vs. Later Anticoagulation for Stroke with AF*

- The incidence of recurrent ischemic stroke, systemic embolism, ICH, or vascular death @ 30 days → 2.8% LOWER to 0.5% HIGHER with early rather than later use of DOACs
- In mild to moderate stroke patients anticoagulation is safe **within 48 hours**