ONLINE SUPPLEMENTAL
for manuscript entitled

Efficacy and safety of bridging thrombolysis initiated before transfer in a drip-and-ship stroke service
Figure SF1. Visualization of occlusion sites and rates of early recanalization according to treatment with bridging thrombolysis (BT) or no-BT. Abbreviations: BA, basilar artery; CSC, comprehensive stroke center; ICA, internal carotid artery; MCA, middle cerebral artery; M1–M3, segments of the MCA; PCA, posterior cerebral artery; VA, vertebral artery.
Full patient cohort analysis including posterior circulation stroke

Definition: Acute ischemic stroke and LVO (internal carotid artery [ICA], carotid T, middle cerebral artery [MCA, segments M1–M3], posterior cerebral artery (PCA), vertebral artery [VA], basilar artery [BA]).

Baseline characteristics
In a total of 442 patients (54.4%) BT was initiated at the referring hospital (table S1). Reasons for not performing BT are listed in table S2. In patients for whom the exact time of stroke onset was known (BT, 87.8% vs. no-BT, 49.7%), time to first recanalization therapy, i.e., intravenous thrombolysis in the BT group, was shorter in the BT group (table S1). High-grade stenosis or occlusion was present in all patients before transfer, with isolated M1 or M2 occlusions being the most frequent occlusion sites (38.8%, and 20%, respectively). Distribution of LVO was similar between patients treated with BT or not (table S1). Thrombus migration was observed more often with BT than without (BT, M1 to M2, n=6, M2 to M3, n=7; no-BT, M1 to M2, n=1, M1 to M3, n=1).

Treatment modalities
Of 442 patients treated with BT, 360 (81.4%) underwent DSA. Of these, 25 (8.2%) did not need any extra- or intracranial endovascular therapy. In those 370 patients in whom BT was not initiated at the referring hospital, 8 patients received intravenous thrombolysis at our comprehensive stroke center (n=3 intravenous thrombolysis only, 0.8%) and in 367 DSA was performed (99.2%), there ultimately being no need for endovascular therapy in 4/367 patients (1.1%).

Efficacy
More patients in the BT group with documented LVO before transfer were recanalized without endovascular therapy (56/442, 12.7%) than patients who did not receive BT before transfer (4/370, 1.1%; p<0.0001) (figure SF1). BT remained the strongest independent predictor of early recanalization in a multivariate analysis (adj. OR 14.55, 95% CI 5.15–41.1, p<0.001; table S3). Time window was excluded from the main model because it constituted a major reason for withholding BT while it otherwise showed a strong correlation with initiation of BT. However, BT remained the strongest independent predictor of early recanalization (adj. OR 10.56, 95% CI 1.4–79.99, p=0.022) in a sensitivity analysis including only patients for whom the exact time window for stroke onset was known < 4.5 h (n=424).
In patients in whom diagnostic or therapeutic DSA was performed, reperfusion grades were similar between patients pretreated with BT and those who were not (excellent reperfusion [mTICI 2c–3], 224/360, 62.2% vs. 219/367, 59.7%; good reperfusion [mTICI 2b] 88/360, 24.4%
vs. 84/367, 22.9%), but no reperfusion was observed more often in non-BT patients ([mTICI 0], BT 25/360, 6.9% vs. non-BT 42/367, 11.4%, p=0.04).

In univariate analysis, patients treated with BT had a better functional outcome at 3 months (BT, median mRS 3 [IQR 2–5] vs. no-BT, 4 [2–6], p=0.023), and more patients had an excellent favorable outcome (mRS 0–1, 22.7% vs. 14.6%, p=0.004). In binary logistic regression analysis adjusting for confounders, BT remained an independent predictor for an excellent favorable outcome (mRS 0–1) or return to prestroke mRS at 3 months (adj. OR 1.42, 95% CI 1.02–1.98, p=0.04; table S3). By excluding patients with posterior circulation stroke or distal MCA occlusion, a trend remained (adj. OR 1.38, 95% CI 0.97–1.96, p=0.077).

**Safety**

Bleeding complications did not differ between patients who received BT and those who did not (table S4 for Heidelberg Bleeding Classification). Fatal intracranial hemorrhage developed in 7/434 (1.6%) patients in the BT group and 4/386 (1.0%) in the non-BT group (p=0.509). There was no difference in overall mortality (25.7% vs. 27.5%, p=0.619).
Table S1 Baseline demographics and clinical characteristics (full cohort)

|                          | Bridging Thrombolysis (BT) | No Bridging Thrombolysis (no-BT) | p-value |
|--------------------------|----------------------------|----------------------------------|---------|
| N (%)                    | 442 (54.4%)                | 370 (45.6%)                      | -       |
| Age, mean yr (SD)        | 74.3 (11.7)                | 75.8 (11.9)                      | 0.073   |
| Women, n (%)             | 238 (53.8%)                | 204 (55.1)                       | 0.724   |
| Comorbidities, n (%)     |                            |                                  |         |
| Arterial hypertension    | 352 (79.6%)                | 298 (80.5%)                      | 0.792   |
| Diabetes mellitus        | 99/441 (22.4%)             | 103 (27.8%)                      | 0.087   |
| Hyperlipidemia           | 152/440 (34.5)             | 140/367 (38.1%)                  | 0.304   |
| Ischemic heart disease   | 119/441 (27%)              | 102/369 (27.4%)                  | 0.874   |
| Peripherial artery disease| 31/440 (7%)               | 33/380 (8.7%)                    | 0.434   |
| Stroke/TIA               | 82/440 (18.6%)             | 96/369 (26%)                     | 0.013   |
| Current Smoker           | 62/428 (14.5%)             | 52/364 (14.3%)                   | >0.99   |
| Atrial fibrillation*     | 178/440 (40.5%)            | 200/368 (54.3%)                  | <0.001  |
| Prestroke mRS median (IQR)| 0 (0–2)                   | 1 (0–3)                          | <0.001  |
| 0–1                      | 308/440 (70.0%)            | 210/367 (57.2%)                  | <0.001  |
| 2–5                      | 132/440 (30.0%)            | 157/367 (42.8%)                  | <0.001  |
| NIHSS, median (IQR)      | 15 (9–21)                 | 15 (8–20)                        | 0.168   |
| ASPECTS, median (IQR)    | 9 (7–10)                  | 9 (8–10)                         | 0.354   |
| Occlusion site, n (%)    |                            |                                  |         |
| ICA                      | 14 (3.2%)                 | 24 (6.5%)                        | 0.03    |
| ICA plus MCA             | 55 (12.4%)                | 44 (11.9%)                       | 0.830   |
| Carotid T                | 64 (14.5%)                | 36 (9.7%)                        | 0.042   |
| MCA, M1                  | 169 (38.2%)               | 146 (39.5%)                      | 0.772   |
| MCA, M2                  | 92 (20.8%)                | 70 (18.9%)                       | 0.538   |
| MCA, M3                  | 2 (0.5%)                  | 1 (0.3%)                         | >0.99   |
| PCA                      | 4 (0.9%)                  | 8 (2.2%)                         | 0.156   |
| BA                       | 38 (8.6%)                 | 42 (10.8%)                       | 0.339   |
| VA                       | 4 (0.9%)                  | 1 (0.3%)                         | 0.383   |
| Time window†, median (IQR)| 1:50 (1:20–2:55)          | 6:38 (4:18–10:25)                | <0.001  |

* known or newly diagnosed; † in patients in whom exact time of onset is known.

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; M1–M3, segments of the MCA; mRS, Modified Rankin scale score; NIHSS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; VA, vertebral artery.
### Table S2 Reasons for not performing thrombolysis at the referring hospital (full cohort)

| Reason                                      | N (%)      |
|---------------------------------------------|------------|
| Unknown time window                         | 110 (29.7%)|
| Anticoagulation                             | 102 (27.6%)|
| Time window ≥ 4.5 h                         | 76 (20.5%) |
| Contraindication to intravenous thrombolysis| 50 (13.5%) |
| Multiple reasons                            | 21 (5.7%)  |
| Unknown reason                              | 6 (1.6%)   |
| Other                                       | 5 (1.4%)   |

### Table S3 Multivariate analyses (full cohort)

#### Predictors of excellent functional outcome

|                          | OR     | 95% CI    | p-value |
|--------------------------|--------|-----------|---------|
| Bridging thrombolysis    | 1.42   | 1.02–1.98 | 0.040   |
| Age                      | 0.98   | 0.96–0.99 | 0.001   |
| Atrial fibrillation      | 1.0    | 0.69–1.43 | 0.980   |
| Diabetes mellitus        | 0.63   | 0.42–0.95 | 0.027   |
| Previous stroke          | 1.08   | 0.72–1.6  | 0.719   |

**Occlusion site**

|                          |         |          |         |
|--------------------------|---------|----------|---------|
| Posterior circulation (BA, PCA, VA) | ref.    |          |         |
| ICA                      | 1.13    | 0.44–2.9 | 0.808   |
| ICA plus MCA             | 1.02    | 0.51–2.05| 0.948   |
| Carotid T                | 0.75    | 0.36–0.59 | 0.456  |
| MCA, M1                  | 1.47    | 0.83–2.58 | 0.183  |
| MCA, M2                  | 2.07    | 1.13–3.8  | 0.019   |
| MCA, M3                  | 8.27    | 0.7–98.29 | 0.094   |

#### Predictors of early recanalization

|                          | OR     | 95% CI    | p-value |
|--------------------------|--------|-----------|---------|
| Bridging thrombolysis    | 14.55  | 5.15–41.1 | <0.001  |
| Age                      | 1.03   | 1.01–1.06 | 0.021   |
| Sex (female)             | 0.82   | 0.46–1.49 | 0.524   |
| Arterial hypertension    | 0.45   | 0.23–0.91 | 0.025   |
| Atrial fibrillation      | 0.85   | 0.47–1.56 | 0.603   |
Diabetes mellitus & 0.73 & 0.35–1.51 & 0.395 \\
Hypercholesterinemia & 1.61 & 0.89–2.89 & 0.115 \\

### Occlusion site

|                          |                  |                  |            |
|--------------------------|------------------|------------------|------------|
| Posterior circulation (BA, PCA, VA) | ref.             |                  |            |
| ICA                      | Did not converge |                  |            |
| ICA plus MCA             | 0.15             | 0.03–0.76        | 0.021      |
| Carotid T                | 0.17             | 0.04–0.7         | 0.014      |
| MCA, M1                  | 0.78             | 0.33–1.84        | 0.574      |
| MCA, M2                  | 0.84             | 0.34–2.09        | 0.706      |

Abbreviations: BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; M1–M2, segments of the MCA; OR, odds ratio.

### Table S4 Intracranial hemorrhages according to the Heidelberg Bleeding Classification (full cohort)

| Class | Type          | Bridging Thrombolysis (BT) | No Bridging Thrombolysis (no-BT) |
|-------|---------------|-----------------------------|----------------------------------|
| 0     | None          | 328 (74.7%)                 | 269 (73.3%)                      |
| 1a    | HI1           | 38 (8.7%)                   | 44 (12%)                         |
| 1b    | HI2           | 10 (2.3%)                   | 16 (4.4%)                        |
| 1c    | PH1           | 16 (3.6%)                   | 9 (2.5%)                         |
| 2     | PH2           | 18 (4.1%)                   | 10 (2.7%)                        |
| 3a    | Remote PH     | 6 (1.4%)                    | 1 (0.3%)                         |
| 3b    | IVH           | 1 (0.2%)                    | 0 (0%)                           |
| 3c    | SAH           | 22 (5.0%)                   | 17 (4.6%)                        |
| 3d    | SDH           | 0 (0%)                      | 0 (0%)                           |
| Other | nonclassified | 0 (0%)                      | 1 (0.3%)                         |

Missing data in n=3 patients in each group. Abbreviations: HI, hemorrhagic infarction; IVH, intraventricular hemorrhage; PH, parenchymal hemorrhage; SAH, subarachnoid hemorrhage; SDH, subdural hematoma.