

# IVT for AIS in cancer patients

## Supplementary Search Strategy

### 1. Medline and Embase (via Ovid):

- #1 cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp "intracranial embolism and thrombosis"/ or stroke/ or exp brain infarction/ or stroke, lacunar/ or vasospasm, intracranial/ or vertebral artery dissection/ 1148813
- #2 (stroke or cerebrovasc\$ or brain vasc\$ or cerebral vasc\$ or cva\$ or apoplex\$).tw. 736696
- #3 ((brain\$ or cerebr\$ or cerebell\$ or intracran\$ or intracerebral) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$)).tw. 254930
- #4 or/1-3 1548502
- #5 exp neoplasm/ 7707737
- #6 (malignan\* or neoplas\* or cancer\* or carcinoma\* or tumor\*).mp. 9378777
- #7 5 or 6 10201173
- #8 thrombolytic therapy/ 46351
- #9 fibrinolytic agents/ or plasmin/ or plasminogen/ or tissue plasminogen activator/ or exp plasminogen activators/ or urokinase-type plasminogen activator/ 175310
- #10 fibrinolysis/ 54839
- #11 (thromboly\$ or fibrinoly\$ or recanaliz\$ or recanaliz\$).tw. 183825
- #12 ((clot\$ or thrombus) adj5 (lyse or lysis or dissolve\$ or dissolution)).tw. 10380
- #13 (tPA or t-PA or rtPA or rt-PA or plasminogen or plasmin or alteplase or actilyse).tw. 155834
- #14 (anistreplase or streptodornase or streptokinase or urokinase or pro?urokinase or rpro?uk or lumbrokinase or duteplase or lanoteplase or pamiteplase or reteplase or saruplase or staphylokinase or streptase or tenecteplase or desmoteplase or retevase).tw. 49608
- #15 or/#8-#14 373378
- #16 #4 and #7 and #15 8133

### 2. The Cochrane Central Register of Controlled Trials (CENTRAL):

- #1 [mh ^"cerebrovascular disorders"] or [mh "basal ganglia cerebrovascular disease"] or [mh "brain ischemia"] or [mh "carotid artery diseases"] or [mh "intracranial arterial diseases"] or [mh "intracranial embolism and thrombosis"] or [mh "intracranial hemorrhages"] or [mh ^stroke] or [mh "brain infarction"] or [mh ^"stroke, lacunar"] or [mh ^"vasospasm, intracranial"] or [mh ^"vertebral artery dissection"] 14341
- #2 (stroke or cerebrovasc\* or brain next vasc\* or cerebral next vasc\* or cva\* or apoplexy\*):ti,ab 52979
- #3 (brain\* or cerebr\* or cerebell\* or intracran\* or intracerebral) near/5 (isch\*emi\* or infarct\* or thrombo\* or emboli\* or occlus\*) 14639
- #4 [mh ^"gait disorders, neurologic"] 609
- #5 #1 or #2 or #3 or #4 61654
- #6 MeSH descriptor Neoplasms explode all trees 559
- #7 malignan\* or neoplas\* or cancer or carcinoma\* or tumor\* 215672
- #8 #6 or #7 215672
- #9 MeSH descriptor (Thrombolytic Therapy) explode all trees 37
- #10 MeSH descriptor (Fibrinolytic Agents) explode all trees 53
- #11 MeSH descriptor (Fibrinolysis) explode all trees 45
- #12 MeSH descriptor (Plasminogen Activators) explode all trees 10
- #13 (plasminogen near/2 activator\* or rt-pa or tPA or \*urokinase or alteplase or reteplase or tenecteplase or saruplase or anistreplase or monteplase or streptokinase or staphylokinase or avelizin or awelysin or cellase or distreptase or Kabikinase or kabivitrin or Streptase or streptodecase or apsc or Abbokinase or renokinase or Actilyse or Activase or Eminase or Retavase or Rapiysin or desmople-tase or u-pa or altimeprase) 8049
- #14 thromboly\* or fibrinoly\* or antithrombotic or antithrombic 13803
- #15 #9 or #10 or #11 or #12 or #13 or #14 17245
- #16 #5 and #8 and #15 195

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3. The US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov)  
Condition/diseases: stroke AND cancer; Other Terms: thrombolysis.  
Results: 0

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**Supplementary Table 1.** Quality assessment of retrospective cohort studies by Newcastle-Ottawa Scale

Items	Schwarz- bach/2012 [1]	Kolb/ 2013 [2]	Murthy/ 2013 [3]	Portilla/ 2014 [4]	Murthy/ 2015 [5]	Sobolews- ki/2015 [6]	Geraldes/ 2017 [7]	Weeda/ 2019 [8]	Selvik/ 2018 [9]	Owusu- Guha/2019 [10]	Sallustio/ 2019 [11]
<b>Selection</b>											
1) Representativeness of the exposed cohort <sup>a</sup>	1	1	1	1	1	1	1	1	1	1	1
2) Selection of the non-exposed cohort <sup>b</sup>	1	1	1	1	1	1	1	1	1	1	1
3) Assessment of the exposure <sup>c</sup>	1	1	1	1	1	1	1	1	1	1	1
4) Outcome of interest not present at the start of the study <sup>d</sup>	1	1	1	1	1	1	1	1	1	1	1
<b>Comparability</b>											
1) Comparability of cohorts based on the design or analysis <sup>e</sup>	-	-	1	-	1	2	1	1	2	1	2
<b>Outcome</b>											
1) Assessment of the outcome <sup>f</sup>	1	1	-	-	1	1	1	1	-	1	1
2) Was follow-up long enough for outcomes to occur <sup>g</sup>	1	1	1	1	1	1	1	1	1	1	1
3) Adequacy of follow up of the cohorts <sup>h</sup>	1	1	1	1	1	1	1	1	1	1	1
<b>Total score</b>	<b>7</b>	<b>7</b>	<b>7</b>	<b>6</b>	<b>8</b>	<b>9</b>	<b>8</b>	<b>8</b>	<b>8</b>	<b>8</b>	<b>9</b>

<sup>a</sup>Star assigned if exposed cohort was truly/somewhat representative of the cancer patients treated with IVT for AIS in the community (i.e., the sample was consecutive or covered all patients in hospital during specific periods). <sup>b</sup>Star assigned where non-exposed participants (non-cancer patients treated with IVT for AIS) were drawn from the same population as the exposed. <sup>c</sup>Star assigned if cancer status had been assessed via structured interview or medical records. <sup>d</sup>Star assigned if outcomes appeared after the initiation of IVT. <sup>e</sup>One star assigned if the study matched for age; Second star assigned if it further matched for baseline NIHSS. <sup>f</sup>Star assigned if outcomes were identified by medical records/CT imaging. <sup>g</sup>Star assigned if it at least followed up till discharge. <sup>h</sup>Star assigned where the loss to follow-up had been estimated and reported in the study, and where loss was no more than 10%. Abbreviations: IVT, intravenous thrombolysis; AIS, acute ischemic stroke; NIHSS, National Institutes of Health Stroke Scale; CT, Computed Tomography.

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**Supplementary Table 2.** Quality assessment of case series by IHE checklist

Checklist items	Lee/ 2011 [12]	Graber/ 2012 [13]	Cappellari/ 2013 [14]	Nam/ 2017 [15]
<b>Study objective</b>				
1. Was the hypothesis/aim/objective of the study clearly stated?	Yes	Yes	Yes	Yes
<b>Study design</b>				
2. Was the study conducted prospectively?	No	No	No	No
3. Were the cases collected in more than one center?	Yes	No	No	Yes
4. Were patients recruited consecutively?	Unclear	Unclear	Yes	Yes
<b>Study population</b>				
5. Were characteristics of the patients in the study described?	No	Yes	Yes	Yes
6. Were eligibility criteria (i.e. inclusion/exclusion) clearly stated?	Partial	Yes	Yes	Yes
7. Did patients enter the study at a similar point in the disease?	Unclear	Unclear	Unclear	Unclear
<b>Intervention and co-intervention</b>				
8. Was the intervention of interest clearly described?	Partial	Partial	Partial	Yes
9. Were additional interventions clearly described?	Yes	No	No	Yes
<b>Outcome measures</b>				
10. Were relevant outcome measures established a priori?	Yes	Yes	No	Yes
11. Were outcome assessors blinded to the intervention?	Unclear	Unclear	Unclear	Unclear
12. Were relevant outcomes measured with appropriate objective or subjective methods?	Yes	Yes	Unclear	Yes
13. Were outcomes measured before and after the intervention?	Unclear	Yes	Unclear	Unclear
<b>Statistical analysis</b>				
14. Were the statistical tests assessing relevant outcomes appropriate?	Unclear	Unclear	Unclear	Yes
<b>Results and conclusions</b>				
15. Was follow-up long enough for events and outcomes to occur?	Yes	Yes	Yes	Yes
16. Were losses to follow-up reported?	Yes	Yes	Yes	Yes
17. Did the study provide estimates of random variability in analysis of relevant outcomes?	No	No	Partial	Partial
18. Were the adverse events reported?	Yes	Yes	Yes	Yes
19. Were the conclusions of the study supported by the results?	Yes	Yes	Yes	Yes
<b>Competing interests and sources of support</b>				
20. Were both competing interests and sources of support reported?	No	Partial	Partial	Partial
Number of yes responses	9	10	8	14

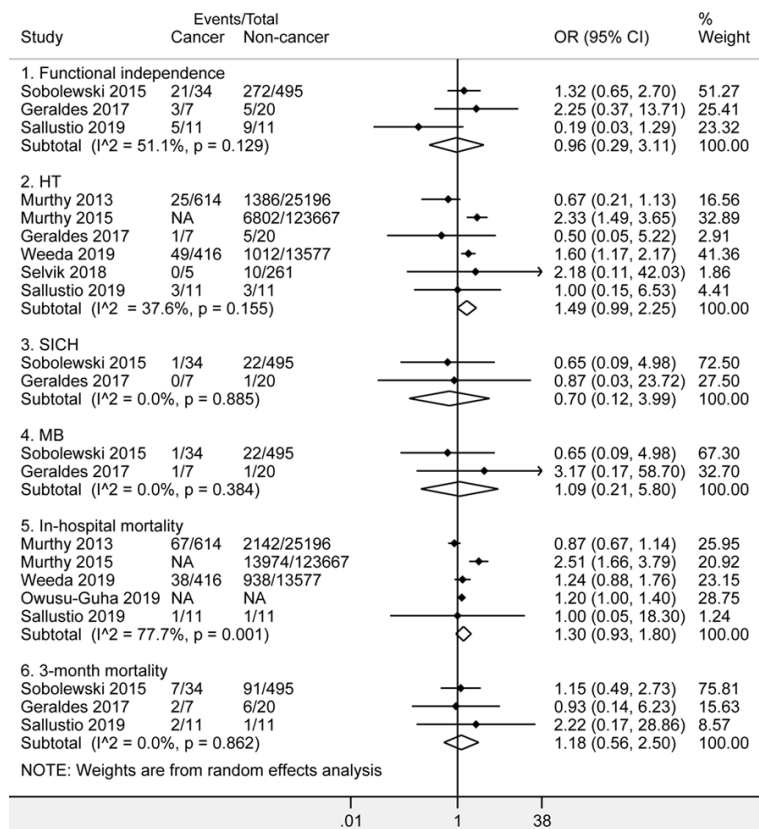
Abbreviations: IHE, Institute of Health Economics.

## References

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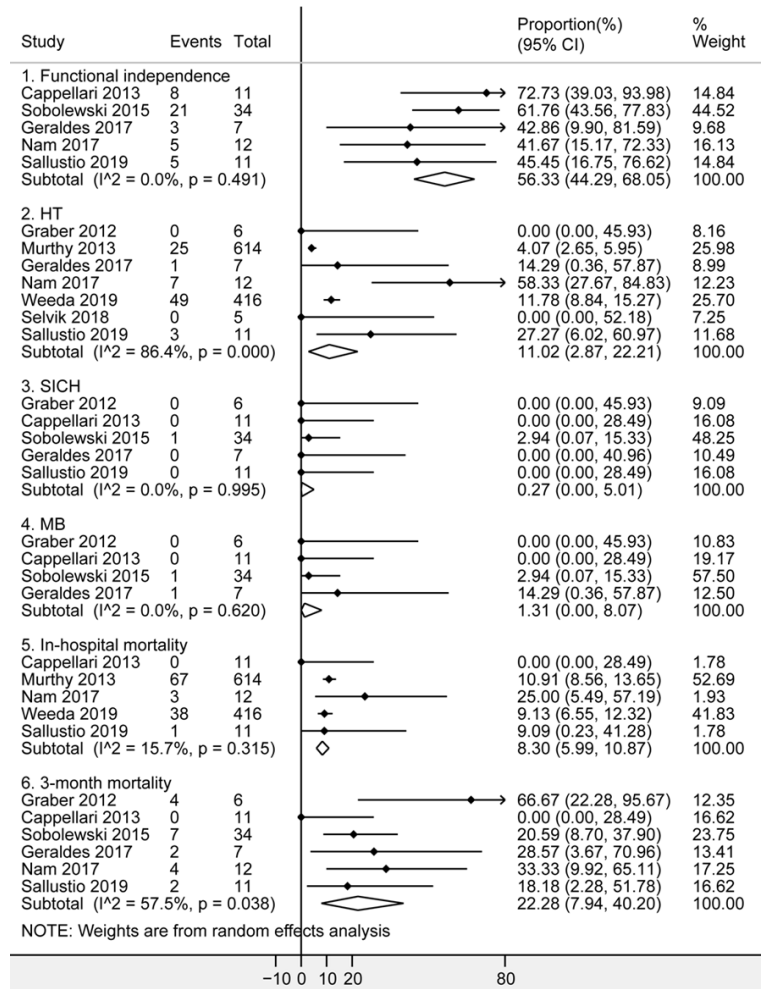
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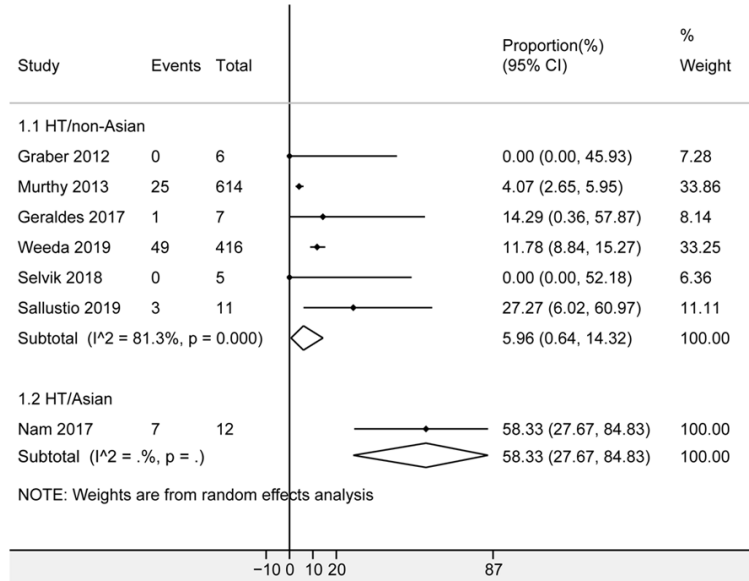
**Supplementary Figure 1.** Forest plots of functional independence, HT, SICH, MB, in-hospital mortality and 3-month mortality after intravenous thrombolysis for acute ischemic stroke in cancer and non-cancer patients (abstracts excluded). The diamond indicated the estimated odds ratio (OR) (95% confidence interval) of cancer to non-cancer patients. The I<sup>2</sup> statistic and p value showed on each figure was for heterogeneity test. Abbreviations: HT, hemorrhagic transformation; SICH, symptomatic intracranial hemorrhage; MB, Major bleeding.

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**Supplementary Figure 2.** Forest plots of functional independence, HT, SICH, MB, in-hospital mortality and 3-month mortality after intravenous thrombolysis for acute ischemic stroke in cancer patients (abstracts excluded). The diamond indicated the estimated proportion (95% confidence interval) in cancer patients. The I<sup>2</sup> statistic and p value showed on each figure was for heterogeneity test. Abbreviations: HT, hemorrhagic transformation; SICH, symptomatic intracranial hemorrhage; MB, Major bleeding.

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**Supplementary Figure 3.** Forest plots of HT after intravenous thrombolysis for acute ischemic stroke in non-Asian and Asian patients with cancer (abstracts excluded). The diamond indicated the estimated proportion (95% confidence interval) in Asian or non-Asian cancer patients. The  $I^2$  statistic and  $p$  value showed on each figure was for heterogeneity test. Abbreviations: HT, hemorrhagic transformation.