Supplementary Material Table 1. Search syntax

| **Number** | **Concept** | **Pubmed Syntax** | **Embase Syntax** | **Cochrane Syntax** |
| --- | --- | --- | --- | --- |
| 1 | Study design | (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti] NOT (animals[mh] NOT humans [mh])) OR (single arm[tiab] OR single-arm[tiab] OR prospective[tiab] OR Phase II[tiab] OR Phase 2[tiab] OR Phase III[tiab] OR Phase 3[tiab] OR observational[tiab]) | ('randomized controlled trial'/de OR 'controlled clinical trial'/de OR 'randomized':ab,ti OR 'placebo':ab,ti OR 'clinical trials'/exp OR 'randomly':ab,ti OR 'trial':ti NOT ('animals'/exp NOT 'humans'/exp)) OR ('single arm':ab,ti OR 'single-arm':ab,ti OR 'prospective':ab,ti OR 'Phase II':ab,ti OR 'Phase 2':ab,ti OR 'Phase III':ab,ti OR 'Phase 3':ab,ti OR 'observational':ab,ti) | - |
| 2 | rrAML | ((((leukaemia[TIAB] OR leukemia[TIAB] OR "Leukemia"[Mesh]) AND (myeloid[TIAB] OR myelogenous[TIAB] OR myeloproliferative[TIAB])) OR "Leukemia, Myeloid"[Mesh]) AND (relaps\*[TIAB] OR refract\*[TIAB])) | (((('leukaemia':ab,ti OR 'leukemia':ab,ti OR 'Leukemia'/exp) AND ('myeloid':ab,ti OR 'myelogenous':ab,ti OR 'myeloproliferative':ab,ti)) OR 'Leukemia, Myeloid'/exp) AND ('relaps$':ab,ti OR 'refract$':ab,ti)) | (relapsed OR refractory) AND (‘acute myeloid leukemia’) |
| 3 | Language | English[lang] | [english]/lim | - |
| 4 | Publication date | ("2000/01/01"[PDAT] : "2020/12/30"[PDAT]) | [2000-2020]/py | 2000--2020 |
| 5 | Final syntax | #1 AND #2 AND #3 AND #4 | #1 AND #2 AND #3 AND #4 | 3,810 |

Supplementary Material Table 2. Eligibility criteria

|  |  |  |
| --- | --- | --- |
| Domain | Inclusion | Exclusion |
|
| Population | * Adult rrAML patients are considered not eligible for intensive therapy if   + Patients had received one of the predefined interventions\*\* , or   + The publication mentions the term ‘not/non/in eligible or ‘unfit’ explicitly in reference to eligibility for intensive therapy, for the included patient population | * Newly diagnosed, front line AML patients * Secondary to any other disease * The study conducted in a mixed population |
| Intervention/  Comparators | * Any treatment suitable for rrAML patients not eligible for intensive therapy, with US or EU label | * Intensive chemotherapies * Treatments suitable for rrAML patients not eligible for intensive therapy, without US or EU label |
| Outcome | * Overall survival * Progression-free survival or similar endpoints * Response * Duration of response * Transplantation rate | Any other outcome out of scope, e.g., health state utility values (HSUV), health care resource use (HCRU), costs, health-related quality of life (HRQoL), prevalence and incidence |
| Study design | * RCTs * Single-arm trials * Observational studies | * Systematic reviews and meta-analysis\* * Case reports, reviews, letters |
| Language | English | Non-English |
| Date | Papers published after 2000  Conference abstracts published from 2017 till 2020 March | Published before 2000  Conference abstracts published before 2017 |
| \* Systematic reviews and meta-analyses were excluded at the title/abstract screening stage. However, the full-texts of there reports were acquired and hand-searched to find any additional relevant primary studies not identified through the database searches  \*\* Interventions were identified through EMA and FDA websites and crosschecked with medical experts. Interventions included were: decitabine, azacytidine, guadecitabine, GO, low-dose cytarabine; rrAML subgroup interventions: gilteritinib (for FLT3 mutation), enasidinib (for IDH2 mutations), ivosidenib (for IDH1 mutations), any licensed intervention if deemed for unfit patients by authors. | | |