Supplementary Material 4. Certainty of evidence from *in vivo* studies.

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| **Outcome** | **Certainty assessment** | | | | | **Certainty** |
| **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** |
| Inhibitory effect on tumor growth [26] | seriousa | not serious | not serious | not serious | dose response gradient | ⨁⨁⨁⨁  High |
| Inhibitory effect on tumor growth[43] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Bcl-2 level reduction [43] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Increased P53 levels [43] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| LDH level reduction [43] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁ |
| CK-MB level reduction [43] | not serious | not serious | not serious | not serious | none | High |
| Inhibitory effect on tumor growth [44] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Increased the number of splenocytes [44] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Increased lymphocytes cells (CD4+ and CD8+) [44] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Increased myeloid cells (granulocytic and monocytic) [44] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Inhibitory effects on tumor growth [45] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Suppression of Notch1, Hes1, JAG1, CTNNB1, VEGF, TNF-α, IL-6, and IFN-γ gene expression [45] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Increased IL-2 gene expression [45] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Increased lymphocytes cells (CD4+ and CD8+) [45] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Increased apoptosis rate [45] | not serious | not serious | not serious | not serious | none | ⨁⨁⨁⨁  High |
| Antiangiogenic effect [35] | seriousa | not serious | not serious | not serious | none | ⨁⨁⨁◯  Moderate |
| Inhibitory effect on tumor growth [36] | seriousa | not serious | not serious | not serious | none | ⨁⨁⨁◯  Moderate |

aThe animal randomization was not detected. Most domains presented uncertainty regarding bias. Bcal-2: B-cell lymphoma 2; LDH: lactate dehydrogenase; CK-MB: creatine kinase-MB; Notch1: Notch 1; Hes1 - hairy and enhancer-of-split 1; Jag1: jagged 1; CTNNB1: cadherin-associated protein beta-1; VEGF: vascular endothelial growth factor; TNF-α: tumor necrosis factor alpha; IL-6: interleukin-6; IFN-γ: Interferon gamma; IL-2: interleukin-2.