

**Supplementary Table S1.** Active and beginning clinical trials against Hepatocellular Carcinoma/Cancer with the drugs Rapamycin, Temsirolimus, Everolimus, AZD8055 and INK128, mainly targeting components of the mTOR pathway. Data provided by clinicaltrials.gov [121].

Abbreviations Status: R-recruiting, N -not yet recruiting, A -active

| Title   | Status | Conditions  | Interventions  | Countries                              |
|---|--------|---|--|--|
| Trametinib Combined With Everolimus and Lenvatinib for Recurrent/Refractory Advanced Solid Tumors   | R      | HCC   | Everolimus inter alia  | China                                  |
| Sirolimus-based Immunosuppression Treatment Regimen for Liver Transplantation   | N      | Liver transplan-<br>tation  | Sirolimus (Rapamy-<br>cin), inter alia   | China                                  |
| MLN0128 Compared to Sorafenib in Advanced or Metastatic Hepatocellular Carcinoma  | A      | HCC   | MLN0128, (RP2D)<br>inter alia  | USA                                    |
| Targeted Therapy Directed by Genetic Testing in Treating Patients With Advanced Refractory Solid Tumors, Lymphomas, or Multiple Myeloma (The MATCH Screening Trial) | R      | Liver and Intra-<br>hepatic Bile Duct<br>Carcinoma,<br>inter alia | Capivasertib, Co-<br>panlisib, Copanlisib<br>Hydrochloride, Ipa-<br>tasertib, PI3K-beta In-<br>hibitor GSK2636771,<br>Sapanisertib,<br>Sunitinib Malate,<br>Taselisib inter alia | USA                                    |
| Risk-Based Therapy in Treating Younger Patients With Newly Diagnosed Liver Cancer   | A      | Hepatoblasoma   | Temsirolimus,<br>inter alia  | USA,<br>Australia,<br>Canada,<br>Japan |

**Supplementary Table S2.** Completed clinical trials against Hepatocellular Carcinoma/Cancer with the drugs Rapamycin, Temsirolimus, Everolimus, AZD8055 and INK128, mainly targeting components of the mTOR pathway. Data provided by clinicaltrials.gov [121].

| Title  | Conditions   | Interventions                    | Countries     |
|--|--|----------------------------------|---------------|
| Temsirolimus and Sorafenib in Advanced Hepatocellular Carcinoma  | Hepatocellular Carcinoma   | Temsirolimus inter alia          | USA           |
| Phase II Combination of Temsirolimus and Sorafenib in Advanced Hepatocellular Carcinoma                                      | Hepatocellular Carcinoma   | Temsirolimus inter alia          | USA           |
| Immunosuppression in Patients Undergoing Liver Transplantation for Hepatocellular Carcinoma                                  | Hepatocellular Carcinoma   | Sirolimus (Rapamycin) inter alia | Germany       |
| Hepatocellular Carcinoma (HCC)_Torisel_  | Inoperable HCC   | Torisel                          | China         |
| Efficacy of Sirolimus In Liver Transplantation for Hepatocellular Carcinoma (HCC)  | Hepatocellular Carcinoma   | Sirolimus (Rapamycin)            | South Korea   |
| Adjuvant Anti-Recurrence Treatment With Rapamycin on Early-stage HCC   | Hepatocellular Carcinoma, Rapamycin  | Rapamycin                        | China         |
| Temsirolimus and Bevacizumab in Treating Patients With Advanced Endometrial, Ovarian, Liver, Carcinoid, or Islet Cell Cancer | Adult Hepatocellular Carcinoma, Advanced Adult Hepatocellular Carcinoma, Localized Non-Resectable Adult Liver Carcinoma, Recurrent Adult Liver Carcinoma, inter alia | Temsirolimus                     | USA, Canada   |
| De Novo Sirolimus-based Immunosuppression After Liver Transplantation for Hepatocellular Carcinoma                           | Liver Carcinoma  | Sirolimus (Rapamycin)            | Canada        |
| Sirolimus and Bevacizumab in Treating Patients With Liver Cancer That Cannot Be Removed by Surgery                           | Liver Cancer   | Rapamycin inter alia             | Singapore     |
| Nivolumab (Opdivo) Plus ABI-009 (Nab-rapamycin) for Advanced Sarcoma and Certain Cancers                                     | Hepatocellular Carcinoma, MTOR Activating Mutation, inter alia   | Rapamycin inter alia             | United States |
| Vaccine Therapy With or Without Sirolimus in Treating Patients With NY-ESO-1 Expressing Solid Tumors                         | Recurrent Hepatocellular Carcinoma, Resectable Hepatocellular Carcinoma, Sarcoma, inter alia   | Sirolimus (Rapamycin) inter alia | USA           |

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|---|---|--|---|
| Study to Assess Safety, Pharmacokinetics, and Efficacy of Oral CC-223 for Patients With Advanced Solid Tumors, Non-Hodgkin Lymphoma or Multiple Myeloma   | Multiforme, Hepatocellular Carcinoma, inter alia    | CC-223   | USA, France, Spain, UK  |
| Safety, Tolerability, Pharmacokinetics (PK) and Preliminary Efficacy of Tor Kinase Inhibitor in Liver Cancer Patients   | Cancer, Advanced Hepatocellular Carcinoma           | AZD8055  | South Korea   |
| Lenalidomide in Combination With Bevacizumab, Sorafenib, Temsirolimus, or 5-Fluorouracil, Leucovorin, Oxaliplatin (FOLFOX)  | Advanced Cancers                                    | Temsirolimus inter alia                          | USA   |
| Everolimus and Pasireotide (SOM230) in Patients With Advanced or Metastatic Hepatocellular Carcinoma  | Advanced Adult Hepatocellular Carcinoma             | Everolimus inter alia                            | USA   |
| Antiangiogenic Treatment of Hepatocellular Cancer With Bevacizumab and RAD001   | Hepatocellular Carcinoma                            | Everolimus                                       | Germany   |
| RAD001 in Advanced Hepatocellular Carcinoma   | Hepatocellular Carcinoma                            | RAD001 (Everolimus)                              | USA   |
| Study of (1) Everolimus, (2) Estrogen Deprivation Therapy (EDT) With Leuprolide + Letrozole and (3) Everolimus + EDT in Patients With Unresectable Fibrolamellar Hepatocellular Carcinoma (FLL-HCC) | Fibrolamellar Carcinoma, Fibrolamellar Liver Cancer | Everolimus, combination of everolimus inter alia | USA   |
| Global Study Looking at the Combination of RAD001 Plus Best Supportive Care (BSC) and Placebo Plus BSC to Treat Patients With Advanced Hepatocellular Carcinoma.                                    | Carcinoma   | Everolimus, Everolimus Placebo                   | USA, Australia, Austria, Belgium, Canada, China, France, Germany, Greece, Hungary, Israel, Italy, Japan, South Korea, Spain, Thailand |
| Sorafenib Tosylate With or Without Everolimus in Treating Patients With Localized, Unresectable, or Metastatic Liver Cancer   | Liver Cancer  | Everolimus, inter alia                           | Austria, Hungary, Switzerland   |
| Circulating Tumor Cells and Tumor DNA in HCC and NET  | Carcinoma, Hepatocellular, Neuroendocrine Tumors    | Everolimus inter alia                            | Denmark   |

|   |                             |                                  |     |
|---|-----------------------------|----------------------------------|-----|
| Rapamycin With Grapefruit Juice for Advanced Malignancies   | Tumors, Neoplasm Metastasis | Rapamycin (Sirolimus)            | USA |
| A Study of CD45RA+ Depleted Haploidentical Stem Cell Transplantation in Children With Relapsed or Refractory Solid Tumors and Lymphomas | Hepatic Tumor, inter alia   | Sirolimus (Rapamycin) inter alia | USA |
| Pasireotide, Everolimus and Selective Internal Radioembolization Therapy for Unresectable Hepatic Metastases                            | Neuroendocrine Tumors       | Everolimus inter alia            | USA |

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121. Zarin, D.A.; Tse, T.; Williams, R.J.; Califf, R.M.; Ide, N.C. The ClinicalTrials.Gov Results Database — Update and Key Issues. *N Engl J Med* **2011**, *364*, 852–860, doi:10.1056/NEJMsa1012065. (accessed 25.01.2022)