**Table I.** General characteristics of asciminib, an allosteric BCR-ABL tyrosine kinase inhibitor, specifically targeting ABL1 myristoyl pocket

|  |  |
| --- | --- |
| Chemical structure |  |
| IUAPC name | N-[4-[chloro(difluoro)methoxy]phenyl]-6-[(3R)-3-hydroxypyrrolidin-1-yl]-5-(1H-pyrazol-5-yl)pyridine-3-carboxamide |
| Molecular formula | C20H18CIF2N5O3 |
| Spectrum of inhibitory activity [43] | Myristoyl pocket of BCR-ABL1 |
| BCR-ABL1 tyrosine kinase inhibitory mode of action | On fusion of ABL1 to BCR, myristoylated N-terminal is lost and ABL1 kinase is activated. By allosterical binding of myristoyl site, asciminib mimics myristate and restores inhibition of BCR-ABL1 kinase activity [47]After binding to myristoyl pocket of ABL1 kinase domain, asciminib induces an inactive conformational change and inhibits kinase activity [45] |
| Half-life time (T1/2) [44, 48] | 5.5 h (40 mg/day)9 hours (200 mg twice a day) |
| Resistant BCR-ABL1 mutants\* [23, 43, 46, 49–51] | **Detected in *in vitro* conditions** | **Emergence in clinical trials** |
| A337VA344PP465SF497F | G109DY115NM244VV289IA337V/TE355GF359VE462KG463D/SP465SV468FS501RI502L |
| Oral dose per day | CP — 80 mg/d or 40 mg twice a day, in a case of T315I BCR::ABL1 mutation dosages up to 200 mg twice a day\*\* |
| Off-target inhibition [44, 48] | Reversible inhibitor of CYP3A4/5, CYP2C8, CYP2C9, CYP2B6, inhibitor of BCRP, Pgp and weak inhibitor of OCT1 |

\**in vitro* and *in vivo;* \*\* not approved in T315I BCR::ABL1 mutation positive cases in Poland; IUAPC — International Union of Pure and Applied Chemistry; BCRP — breast cancer resistance protein; Pgp — glycoprotein P; OCT1 — organic cation transporter 1