

Study name	Drug observed and number of participants in study arm	Other adverse effects that occurred $\geq 5\%$	Neuropsychiatric adverse effects reported*
Cahn, et al., 2014	dolutegravir (n=357)	diarrhea (20%), upper respiratory tract infection (11%), headache (9%), nausea (8%), cough (9%), influenza (7%), nasopharyngitis (6%), vomiting (6%), rash (5%), upper abdominal pain (5%)	depression (0.6%), suicidal behavior (1.7%)
Dooley, et al., 2019	dolutegravir (n=69)	headache (13%), arthralgia (10%), upper respiratory tract infection (7%), vomiting (7%)	depression (0.6%), dizziness (4.3%), insomnia (2.9%)
Llibre et al., 2018	dolutegravir/rilpivirine (n=513)	nasopharyngitis (10%), headache (8%), upper respiratory tract infection (5%), diarrhea (6%)	anxiety (2.1%), depression (3.3%), dizziness (1.9%), insomnia (3.3%), suicidal behavior (0.6%)
Molina, et al., 2015	dolutegravir (n=242)	diarrhea (18%), nausea (17%), headache (17%), nasopharyngitis (12%), cough (7%), pyrexia (7%), vomiting (6%), back pain (6%), fatigue (6%), rash (5%), bronchitis (5%), gastroenteritis (5%), pharyngitis (5%), abdominal pain (5%), constipation (5%)	anxiety (6.2%), depression (6.6%), dizziness (5.8%), insomnia (7.9%), suicidal behavior (1.7%)
Molina, et al., 2018	dolutegravir (n=281)	respiratory tract infection (10%), diarrhea (9%), nasopharyngitis (7%), headache (7%)	insomnia (5%), suicidal behavior (0.4%)
NCT00543725 (THRIVE)	rilpivirine (n=340)	nausea (17%), diarrhea (14%), vomiting (6.5%), fatigue (5.9%), nasopharyngitis (15%), upper respiratory tract infection (13%), bronchitis (9.1%), influenza (9.4%), pharyngitis (5.9%), anogenital warts (5%), sinusitis (5%), headache (18%), cough (9.7%), pharyngolaryngeal pain (6%)	depression (7.6%), dizziness (12.6%), insomnia (11.2%), suicidal behavior (0.3%)
NCT00540449 (ECHO)	rilpivirine (n=346)	nausea (13%), diarrhea (15%), fatigue (5.8%), upper respiratory tract infection (15%), nasopharyngitis (13%), influenza (11%), back pain (6.7%), headache (15%), cough (6.7%), rash (7.5%)	anxiety (2.7%), depression (8.1%), dizziness (8.1%), insomnia (10%), suicidal behavior (1.2%)
NCT01263015 (SINGLE)	dolutegravir (n=414)	diarrhea (23%), nausea (17%), vomiting (6.8%), fatigue (16%), pyrexia (6.5%), nasopharyngitis (21%), upper respiratory tract infection (17%), bronchitis (8%), sinusitis (7%), influenza (7.5%), back pain (8.9%), arthralgia (6.8%), pain in extremity (5.6%), anogenital warts (5.6%), cough (9.4%), oropharyngeal pain (7.7%), rash (5.3%)	anxiety (8%), depression (8.5%), dizziness (10%), insomnia (18%), suicidal behavior (1.2%)

NCT01709084 (SALIF)	rilpivirine (n=213)	upper respiratory tract infection (30%), urinary tract infection (14%), increased appetite (5.2%), arthralgia (8%), back pain (9.4%), cough (8.9%), pruritis (6.6%)	dizziness (3.3%)
NCT02227238	dolutegravir (n=314)	diarrhea (8.9%), upper respiratory tract infection (14%), headache (7.6%)	depression (0.3%), dizziness (2.9%), insomnia (2.5%), suicidal behavior (0.3%)
NCT02607930	dolutegravir (n=315)	abdominal pain (6.7%), constipation (5.4%), diarrhea (18%), nausea (24%), vomiting (7.6%), fatigue (12%), pyrexia (5.7%), seasonal allergy (5.1%), bronchitis (9.5%), gastroenteritis (7%), gonorrhoea (6.7%), nasopharyngitis (16.5%), pharyngitis (7%), sinusitis (7.3%), syphilis (16%), upper respiratory tract infection (19%), arthralgia (9.2%), back pain (12%), musculoskeletal pain (5.1%), anogenital warts (6%), cough (6.4%), rash (7.6%), oropharyngeal pain (11%)	anxiety (6.3%), depression (8.9%), dizziness (6%), insomnia (11.1%), suicidal behavior (1.3%)
NCT02607956	dolutegravir (n=325)	abdominal pain (5.9%), diarrhea (16%), nausea (13%), vomiting (6.2%), fatigue (11%), pyrexia (9.2%), bronchitis (8.3%), nasopharyngitis (19%), upper respiratory tract infection (16%), arthralgia (7.1%), back pain (12%), musculoskeletal pain (5.5%), headache (18%), cough (8.6%), oropharyngeal pain (5.5%), rash (7.1%)	anxiety (7.7%), depression (8.6%), dizziness (6%), insomnia (7.4%), suicidal behavior (0.6%)
NCT03110380	dolutegravir (n=281)	diarrhea (11%), nasopharyngitis (10%), upper respiratory tract infection (11%) arthralgia (6.1%), headache (8.2%), cough (5.7%)	insomnia (3.9%)
Orrell, et al., 2017	dolutegravir (n=248)	nausea (13%), headache (2%), diarrhea (5%)	anxiety (2%), depression (3.2%), dizziness (5.2%), insomnia (4%), suicidal behavior (1.6%)
Raffi, et al., 2013	dolutegravir (n=411)	nausea (15%), nasopharyngitis (13%), diarrhea (14%), and headache (14%)	anxiety (5.4%), depression (7.5%), dizziness (6.1%), insomnia (6.8%), suicidal behavior (1%)
Stellbrink, et al., 2013	dolutegravir (n=51)	nausea (55%), diarrhea (12%), headache (10%), fatigue (2%)	anxiety (3.9%), depression (3.9%), dizziness (5.9%), insomnia (5.9%)
Trottier, et al., 2017	dolutegravir (n=276)	urinary tract infection (8%), nausea (10%), fatigue (7%), diarrhea (6%), headache (5%), cough (5%)	insomnia (3.6%)

Vera, et al., 2019	rilpivirine (n=37)	headache (19%)	anxiety (41%), depression (46%), dizziness (14%), insomnia (51%),
Wilkins, et al., 2015	rilpivirine (n=394)	diarrhea (18%), nausea (17%), vomiting (5.1%), flatulence (6.1%), fatigue (11%), upper tract infection (15%), nasopharyngitis (8.4%), bronchitis (8.6%), sinusitis (7.1%), syphilis (6.6%), arthralgia (7.1%), back pain (5.1%), myalgia (5.1%), cough (9.6%), oropharyngeal pain (5.8%), rash (7.9%)	anxiety (7.1%), depression (9.6%), dizziness (6.9%), insomnia (11%), suicidal behavior (0.8%)

Footnote:

Neuropsychiatric side-effects definitions*

- **Anxiety defined as:** anxiety, nervousness, panic attacks, panic reaction, and anxiety disorder
- **Depression defined as:** insomnia, restlessness, difficulty sleeping, initial insomnia, middle insomnia, and terminal insomnia
- **Dizziness defined as:** dizziness, lightheadedness, and dizziness postural
- **Insomnia defined as:** insomnia, restlessness, difficulty sleeping, initial insomnia, middle insomnia, and terminal insomnia
- **Suicidal behavior defined as:** suicide attempt, suicide ideation, suicidal behavior, and complete suicide

Table S2: Comparing other adverse effects with neuropsychiatric adverse effects of dolutegravir, rilpivirine, or dolutegravir/rilpivirine